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(54) Title: COMPOSITIONS AND METHODS RELATING TO HEPATIC SPECIFIC GENES AND PROTEINS

(57) Abstract: The present invention relates to newly identified nucleic acid molecules and polypeptides present in normal and neoplastic hepatic cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions containing the nucleic acid molecules, polypeptides, antibodies, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating hepatic cancer and non-cancerous disease states in hepatic, identifying hepatic tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered hepatic tissue for treatment and research.

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COMPOSITIONS AND METHODS RELATING TO HEPATIC SPECIFIC GENES AND PROTEINS

This application claims the benefit of priority from U.S. Provisional Application
5 No. 60/343,137, filed December 21, 2001, which is herein incorporated by reference in its
entirety.

FIELD OF THE INVENTION

The present invention relates to newly identified nucleic acids and polypeptides
present in normal and neoplastic liver and/or hepatic cells, including fragments, variants
10 and derivatives of the nucleic acids and polypeptides. The present invention also relates to
antibodies to the polypeptides of the invention, as well as agonists and antagonists of the
polypeptides of the invention. The invention also relates to compositions comprising the
nucleic acids, polypeptides, antibodies, post translational modifications (PTMs), variants,
derivatives, agonists and antagonists of the invention and methods for the use of these
15 compositions. These uses include identifying, diagnosing, monitoring, staging, imaging
and treating hepatic cancer and non-cancerous disease states in hepatic, identifying hepatic
tissue and monitoring and identifying and/or designing agonists and antagonists of
polypeptides of the invention. The uses also include gene therapy, therapeutic molecules
including but limited to antibodies or antisense molecules, production of transgenic
20 animals and cells, and production of engineered hepatic tissue for treatment and research.

BACKGROUND OF THE INVENTION

While relatively rare in the United States and Canada, hepatocellular carcinoma
(HCC) is the eighth-most common cancer and the leading cause of cancer death in the
world. Yu, M.C. *et al.*, *Can. J. Gastroenterol.* 14(8): 703-09 (2000); Bookstein, R. *et al.*,
25 *Semin. Oncol.* 23(1): 66-77 (1996). Malignant primary hepatic tumors constitute two to
three percent of primary cancers in the United States, with HCC accounting for 90% of
malignant primary tumors of the liver in adults. Anderson, B.B. *et al.*, *J. Nat'l Med. Ass'n*
84(2): 129-35 (1992). Outside of North America, regions of the world particularly at risk
are the East, Southeast Asia, and sub-Saharan Africa. Yu *et al.*, *supra*. In China, for
30 example, HCC is the second-most cause of cancer mortality, accounting for 130,000
deaths annually. Tang, Z.Y. *et al.*, *Ann. Chir.* 52(6): 558-63 (1998). HCC is now
becoming a serious problem in the United States, principally due to patients with cirrhosis

secondary to the hepatitis C virus developing liver cancer. Jeffers, L., *J. Nat'l Med. Ass'n* 92(8): 369-71 (2000).

Although our understanding of the etiology of HCC is undergoing continual refinement, research in this area points to a number of risk factors. In developed countries with populations at low risk for liver cancer, the hepatitis B virus (HBV) and hepatitis C virus (HCV) may be responsible for up to 75% of all liver cancer; in developing countries where HBV is prevalent, it may account for 60% of cases, with HCV playing a role in less than 10% of cases. F. Xavier Bosch, *Global Epidemiology of Hepatocellular Carcinoma, in Liver Cancer* 23 (Kunio Okuda & Edward Tabor, eds. 1997); see also Pei-Jer Chen & Ding-Shinn Chen, *Hepatitis B Virus and Hepatocellular Carcinoma, in Liver Cancer* 29 (Kunio Okuda & Edward Tabor, eds. 1997). Cirrhosis, which is considered by some to be a preneoplastic condition, is associated with three fourths of HCC cases. Swan N. Thung and Michael A. Gerber, *Cirrhosis and Hepatocellular Carcinoma, in Liver Cancer* 155 (Kunio Okuda & Edward Tabor, eds. 1997). Alcohol consumption and cigarette smoking are both risk factors for liver cancer, with a combined 1.2 to 2-fold risk, although cigarette smoking is thought to play a relatively minor role. Bosch, *supra* at 23-24. In developed countries, oral contraceptives have been linked to a two-fold to five-fold risk of liver cancer; in countries where HBV is relatively rare, the long-term usage of oral contraceptives may be responsible for as many as half of all liver cancer cases in women. *Id.* at 24. In Africa and certain areas of China and Southeast Asia, the incidence of liver cancer is correlated with predictions of the consumption of aflatoxin, a carcinogenic DNA intercalator generated by molds growing on spoiled food. *Id.* at 25; Gerald N. Wogan, *Aflatoxin Exposure as a Risk Factor in the Etiology of Hepatocellular Carcinoma, in Liver Cancer* 51 (Kunio Okuda & Edward Tabor, eds. 1997).

Despite recent progress in understanding the molecular and genetic causes of HCC, our understanding of these factors is nonetheless limited. Michael Geissler *et al.*, *Molecular Mechanisms of Hepatocarcinogenesis, in Liver Cancer* 59 (Kunio Okuda & Edward Tabor, eds. 1997). Researchers have theorized that abnormal expression of proto-oncogenes, or the expression of mutant variations of these genes (oncogenes), may lead to the transformation of neoplasms. *Id.* Moreover, induction of apoptosis and alteration of the "p53 tumor suppressor gene-dependent cell cycle checkpoint function" are thought to be involved in HCC as well. *Id.* It has also been postulated that DNA hypomethylation may work as an epigenetic mechanism that participates in the transformation of

hepatocytes. *Id.* Research is currently being performed to determine the possible role HBV and HCV in interfering with the proper function of tumor suppressor genes and in causing mutations in those genes. Edward Tabor, *The Role of Tumor Suppressor Genes in the Development of Hepatocellular Carcinoma*, in Liver Cancer 89 (Kunio Okuda &

- 5 Edward Tabor, eds. 1997). Research is also exploring how liver inflammation and cirrhosis caused by HCV may act as “promoters” in the progression of HCC. *Id.*

The links between certain genetic and acquired diseases of liver metabolism and liver cancer, however, are well-established, particularly those diseases in which chronic liver injury and cirrhosis are hallmark features. Geissler *et al.*, *supra* at 60-61; Yves

10 Deugnier & Bruno Turlin, *Other Causes of Hepatocellular Carcinoma*, in Liver Cancer 97 (Kunio Okuda & Edward Tabor, eds. 1997). These diseases include (1) hematochromatosis, (2) α 1-antitrypsin deficiency, which results from a variant gene on chromosome 14q3, (3) type I tyrosinemia, (4) porphyria cutanea tarda, and (5) alcoholic cirrhosis. Geissler, *supra* at 60; Deugnier & Turlin, *supra* at 102.

- 15 Like many cancers, HCC is more readily treatable when detected early. Michael C. Kew, *Clinical and Nonimaging Diagnosis of Hepatocellular Carcinoma*, in Liver Cancer 315 (Kunio Okuda & Edward Tabor, eds. 1997). Unfortunately, screening for liver cancer is made difficult because symptoms and physical signs of the disease do not occur until its very late stages. *Id.* The absence of clinical manifestations of early-stage
- 20 liver cancer may be attributable to several factors: (1) the position of the liver deep in the peritoneal cavity, such that tumors cannot be readily felt, (2) the liver’s vast functional reserves, which do not allow symptoms to appear until much of the organ has been replaced by carcinoma, and (3) HCC metastasizes in the late stages of the disease. *Id.*

- Routine screening for HCC typically involves the use of ultrasound, in
- 25 combination with the determination of serum levels of α -fetoprotein (AFP). Walter J. Burdette, *Cancer: Etiology, Diagnosis, and Treatment* 108 (1998); Yang, B. *et al.*, *J. Cancer Res. Clin. Oncol.* 123(6): 357-60 (1997). Due to its ability to provide (1) excellent contrast resolution, (2) multiplanar images, and (3) characterization of cancerous lesions based on signal intensities in a variety of pulse sequences, magnetic resonance
- 30 imaging (MRI) is becoming the modality of choice for screening patients for HCC. Sharma, R. & Saini, S., *J. Comput. Assist. Tomogr.* 23 Suppl. 1: S39-44 (1999); Masaaki Ebara, *MRI Diagnosis of Hepatocellular Carcinoma*, in Liver Cancer 361 (Kunio Okuda & Edward Tabor, eds. 1997). Computed tomography (CT) has also proven effective at

detecting HCC, particularly in cases where ultrasound is ineffective due to scar tissue, intervening bones, or air in the gut. Nyung Ihn Choi, *CT Diagnosis of Liver Cancer*, in Liver Cancer 371 (Kunio Okuda & Edward Tabor, eds. 1997). In fact, contrast-enhanced CT's ability to diagnose HCC does not differ significantly from MRI, although MRI is slightly superior in locating cancerous lesions that are 2 cm or smaller. *Id.* at 363. Hepatic angiography, while supplanted to some extent by ultrasound, CT, and MRI, remains useful in preoperative evaluation and in providing vascular maps. Kenichi Takayasu, *Hepatic Angiography*, in Liver Cancer 347 (Kunio Okuda & Edward Tabor, eds. 1997).

10 While a highly sensitive and specific marker would significantly facilitate HCC screening, no such marker has been discovered. Kew, *supra* at 325. Elevated serum level of AFP is a useful diagnostic indicator of HCC, but it is susceptible to false positives and false negatives. *Id.* at 325-26. Des- γ -carboxy prothrombin has been touted as a "better" HCC marker than AFP, but one study reports that AFP is both more sensitive and more specific than des- γ -carboxy prothrombin. *Id.* at 327. Tumor-associated isozymes of γ -glutamyl transferase, which are not detectable in normal serum, are highly specific but lack sensitivity. *Id.* While a number of other markers have been studied, none are sufficiently specific and sensitive to use in routine screening of HCC. *Id.* at 327-28.

20 Once HCC has been diagnosed, treatment decisions are made in reference to the stage of cancer progression. A number of the techniques employed to stage HCC are identical to those used to screen for HCC, including ultrasound, MRI, and CT. Hann, L.E. *et al.*, *Semin. Surg. Oncol.* 19(2): 94-115 (2000). With the use of tissue-specific contrast reagents, MRI has begun to undermine the role of CT portography in preoperative staging, and may soon completely supplant it. Sharma & Saini, *supra*. Researchers have also found that laparoscopy, in combination with laparoscopic ultrasonography, is also effective in preoperative staging. Gouma, D.J. *et al.*, *Scand. J. Gastroenterol. Suppl.* 218: 43-9 (1996). As in the case of screening, highly sensitive and specific markers would be of great assistance in staging HCC, yet none are presently available. Researchers have explored the use of soluble intercellular adhesion molecule-1, soluble interleukin-2 receptor, interleukin 6, and anti-p53, but none of these potential markers was found useful. Parasole, R. *et al.*, *Clin. Cancer Res.* 7(11): 3504-09 (2001).

Several classification systems for staging hepatic cancer are currently used, including the TNM and the Okuda systems. Farinati, F. *et al.*, *Cancer* 89(11): 2266-73

(2000). The TNM system, devised by the Union Internationale Contre le Cancer, is divided into several stages, each of which evaluates the extent of cancer growth with respect to primary tumor (T), regional lymph nodes (N), and distant metastasis (M). Fleming *et al.* eds., *supra* at 3. The TNM system will be discussed in further detail here.

5 Stage 1 is characterized by a single tumor of 2 cm or less in greatest dimension, without vascular invasion (T1), with no regional lymph node metastasis (N0) and no distant metastasis (M0). *Id.* at 94-95. Stages II and IIIA differ from stage I only with respect to tumor category. *Id.* Stage II involves tumor category T2, which may be either (1) a single tumor of 2 cm or less in greatest dimension, with vascular invasion, (2)
10 multiple tumors in only one lobe, all 2 cm or less in greatest dimension, with no vascular invasion, or (3) a single tumor of more than 2 cm in greatest dimension, without vascular invasion. *Id.* Stage IIIA involves tumor category T3, which may be either (1) a single tumor of 2 cm or more in greatest dimension, with vascular invasion, (2) multiple tumors in only one lobe, all 2 cm or less in greatest dimension, with vascular invasion, or (3)
15 multiple tumors in only one lobe, any of which are more than 2 cm in greatest dimension, with or without vascular invasion. *Id.*

 Stage IIIB involves any one of the T1, T2, or T3 categories, metastasis to regional lymph nodes (N1), but no distant metastasis (M0). Stage IVA is characterized by tumor category T4, which may be either (1) multiple tumors in more than one lobe of the liver,
20 (2) involvement of a major branch of the portal or hepatic veins, (3) invasion of nearby organs other than the gallbladder, or (4) perforation of the visceral peritoneum, and any N category with no distant metastasis (M0). *Id.* Lastly, stage IVB involves any T category, any N category, and distant metastasis (M1). *Id.*

 Once the HCC has been staged, typical treatment includes resection, percutaneous
25 ethanol injection, and transcatheter arterial embolization. Shuichi Okada, *Chemotherapy for Hepatocellular Carcinoma*, in Liver Cancer 441 (Kunio Okuda & Edward Tabor, eds. 1997). Indeed, surgical resection of the carcinoma(s) is the first line of treatment for HCC, assuming that no extra-hepatic metastasis has been identified, Kunio Okuda *et al.*, *Treatment Selection*, in Liver Cancer 436 (Kunio Okuda & Edward Tabor, eds. 1997), and
30 transplantation should always be considered in managing HCC, Burdette, *supra* at 111. Treatment with radiation, chemotherapeutics, hormones, and interferon have not proven consistently effective in curing HCC. Llovet, J.M. *et al.*, *Liver Transpl.* 6(6 Suppl. 2): S11-5 (2000). As for radiation, the amount of radiation necessary to achieve an adequate

response may be more than healthy hepatic cells can tolerate, Burdette, *supra* at 113, and as for chemotherapy, no individual anticancer agent or regimen of agents displays a response rate exceeding 20%, Okada, *supra* at 441.

New approaches involving immunotherapy are also being investigated, and these approaches fall within two general categories: specific immunotherapy and nonspecific immunotherapy. Daniel Shouval, *Immunotherapy for Hepatocellular Carcinoma, in Liver Cancer* 471 (Kunio Okuda & Edward Tabor, eds. 1997). As for specific strategies, researchers have targeted HCCs via monoclonal or polyclonal antibodies which recognize antigens on the cancer cell surface; these antibodies are either “free” or are joined to chemotherapeutic or biological molecules. *Id.* As for nonspecific strategies, researchers have explored using interferon- α and γ , lymphokine-activated killer cells, tumor necrosis factor, and antibodies bound to radioactive isotopes. *Id.* While promising, these strategies are still experimental, with much research yet to be done before they can become part of a standard treatment regimen for HCC. *Id.* at 477.

From the foregoing, it is clear that procedures used for detecting, diagnosing, monitoring, staging, prognosticating, and preventing the recurrence of HCC are of critical importance to the outcome of the patient. Moreover, current procedures, while helpful in each of these analyses, are limited by their specificity, sensitivity, invasiveness, and/or their cost. As such, highly specific and sensitive procedures that would operate by way of detecting novel markers in cells, tissues, or bodily fluids, with minimal invasiveness and at a reasonable cost, would be highly desirable.

Accordingly, there is a great need for more sensitive and accurate methods for predicting whether a person is likely to develop HCC, for diagnosing HCC, for monitoring the progression of the disease, for staging HCC, for determining whether HCC has metastasized, and for imaging HCC. There is also a need for better treatment of HCC.

SUMMARY OF THE INVENTION

The present invention solves many needs in the art by providing nucleic acid molecules, polypeptides and antibodies thereto, variants and derivatives of the nucleic acids and polypeptides, agonists and antagonists that may be used to identify, diagnose, monitor, stage, image and treat hepatic cancer and non-cancerous disease states in hepatic; identify and monitor hepatic tissue; and identify and design agonists and antagonists of polypeptides of the invention. The invention also provides gene therapy, methods for

producing transgenic animals and cells, and methods for producing engineered hepatic tissue for treatment and research.

One aspect of the present invention relates to nucleic acid molecules that are specific to hepatic cells, hepatic tissue and/or the hepatic organ. These hepatic specific nucleic acids (HSNAs) may be a naturally occurring cDNA, genomic DNA, RNA, or a
5 fragment of one of these nucleic acids, or may be a non-naturally occurring nucleic acid molecule. If the HSNA is genomic DNA, then the HSNA is a hepatic specific gene (HSG). If the HSNA is RNA, then it is a hepatic specific transcript encoded by a HSG. Due to alternative splicing and transcriptional modification one HSG may encode for
10 multiple hepatic specific RNAs. In a preferred embodiment, the nucleic acid molecule encodes a polypeptide that is specific to hepatic. More preferred is a nucleic acid molecule that encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 410-611. In another preferred embodiment, the nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1-409. For the HSNA sequences listed herein,
15 DEX0374_001.nt.1 corresponds to SEQ ID NO: 1. For sequences with multiple splice variants, the parent sequence DEX0374_001.nt.1, will be followed by DEX0374_001.nt.2, etc. for each splice variant. The sequences off the corresponding peptides are listed as DEX0374_001.aa.1, etc. For the mapping of all of the nucleotides and peptides, see the table in the Example 1 section below.

20 This aspect of the present invention also relates to nucleic acid molecules that selectively hybridize or exhibit substantial sequence similarity to nucleic acid molecules encoding a Hepatic Specific Protein (HSP), or that selectively hybridize or exhibit substantial sequence similarity to a HSNA. In one embodiment of the present invention the nucleic acid molecule comprises an allelic variant of a nucleic acid molecule encoding
25 a HSP, or an allelic variant of a HSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid sequence that encodes a HSP or a part of a nucleic acid sequence of a HSNA.

In addition, this aspect of the present invention relates to a nucleic acid molecule further comprising one or more expression control sequences controlling the transcription
30 and/or translation of all or a part of a HSNA or the transcription and/or translation of a nucleic acid molecule that encodes all or a fragment of a HSP.

Another aspect of the present invention relates to vectors and/or host cells comprising a nucleic acid molecule of this invention. In a preferred embodiment, the

nucleic acid molecule of the vector and/or host cell encodes all or a fragment of a HSP. In another preferred embodiment, the nucleic acid molecule of the vector and/or host cell comprises all or a part of a HSNA. Vectors and host cells of the present invention are useful in the recombinant production of polypeptides, particularly HSPs of the present invention.

Another aspect of the present invention relates to polypeptides encoded by a nucleic acid molecule of this invention. The polypeptide may comprise either a fragment or a full-length protein. In a preferred embodiment, the polypeptide is a HSP. However, this aspect of the present invention also relates to mutant proteins (muteins) of HSPs, fusion proteins of which a portion is a HSP, and proteins and polypeptides encoded by allelic variants of a HSNA as provided herein.

Another aspect of the present invention relates to antibodies and other binders that specifically binds to a polypeptide of the instant invention. Accordingly antibodies or binders of the present specifically bind to HSPs, muteins, fusion proteins, and/or homologous proteins or a polypeptides encoded by allelic variants of an HSNA as provided herein.

Another aspect of the present invention relates to agonists and antagonists of the nucleic acid molecules and polypeptides of this invention. The agonists and antagonists of the instant invention may be used to treat hepatic cancer and non-cancerous disease states in hepatic and to produce engineered hepatic tissue.

Another aspect of the present invention relates to methods for using the nucleic acid molecules to detect or amplify nucleic acid molecules that have similar or identical nucleic acid sequences compared to the nucleic acid molecules described herein. Such methods are useful in identifying, diagnosing, monitoring, staging, imaging and treating hepatic cancer and non-cancerous disease states in hepatic. Such methods are also useful in identifying and/or monitoring hepatic tissue. In addition, measurement of levels of one or more of the nucleic acid molecules of this invention may be useful for diagnostics as part of panel in combination with known other markers, particularly those described in the hepatic cancer background section above.

Another aspect of the present invention relates to use of the nucleic acid molecules of this invention in gene therapy, for producing transgenic animals and cells, and for producing engineered hepatic tissue for treatment and research.

Another aspect of the present invention relates to methods for detecting polypeptides this invention, preferably using antibodies thereto. Such methods are useful to identify, diagnose, monitor, stage, image and treat hepatic cancer and non-cancerous disease states in hepatic. In addition, measurement of levels of one or more of the polypeptides of this invention may be useful to identify, diagnose, monitor, stage, image hepatic cancer in combination with known other markers, particularly those described in the hepatic cancer background section above. The polypeptides of the present invention can also be used to identify and/or monitor hepatic tissue, and to produce engineered hepatic tissue.

Yet another aspect of the present invention relates to a computer readable means of storing the nucleic acid and amino acid sequences of the invention. The records of the computer readable means can be accessed for reading and displaying of sequences for comparison, alignment and ordering of the sequences of the invention to other sequences. In addition, the computer records regarding the nucleic acid and/or amino acid sequences and/or measurements of their levels may be used alone or in combination with other markers to diagnose hepatic related diseases.

DETAILED DESCRIPTION OF THE INVENTION

Definitions and General Techniques

Unless otherwise defined herein, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally, nomenclatures used in connection with, and techniques of, cell and tissue culture, molecular biology, immunology, microbiology, genetics and protein and nucleic acid chemistry and hybridization described herein are those well known and commonly used in the art. The methods and techniques of the present invention are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated. *See, e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual*, 2d ed., Cold Spring Harbor Laboratory Press (1989) and Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 3d ed., Cold Spring Harbor Press (2001); Ausubel et al., *Current Protocols in Molecular Biology*, Greene Publishing Associates

(1992, and Supplements to 2000); Ausubel *et al.*, Short Protocols in Molecular Biology: A Compendium of Methods from Current Protocols in Molecular Biology – 4th Ed., Wiley & Sons (1999); Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1990); and Harlow and Lane, Using Antibodies: A Laboratory Manual,
 5 Cold Spring Harbor Laboratory Press (1999).

Enzymatic reactions and purification techniques are performed according to manufacturer's specifications, as commonly accomplished in the art or as described herein. The nomenclatures used in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and
 10 pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

The following terms, unless otherwise indicated, shall be understood to have the following meanings:

15 A "nucleic acid molecule" of this invention refers to a polymeric form of nucleotides and includes both sense and antisense strands of RNA, cDNA, genomic DNA, and synthetic forms and mixed polymers of the above. A nucleotide refers to a ribonucleotide, deoxynucleotide or a modified form of either type of nucleotide. A "nucleic acid molecule" as used herein is synonymous with "nucleic acid" and
 20 "polynucleotide." The term "nucleic acid molecule" usually refers to a molecule of at least 10 bases in length, unless otherwise specified. The term includes single and double stranded forms of DNA. In addition, a polynucleotide may include either or both naturally occurring and modified nucleotides linked together by naturally occurring and/or non-naturally occurring nucleotide linkages.

25 Nucleotides are represented by single letter symbols in nucleic acid molecule sequences. The following table lists symbols identifying nucleotides or groups of nucleotides which may occupy the symbol position on a nucleic acid molecule. See Nomenclature Committee of the International Union of Biochemistry (NC-IUB), Nomenclature for incompletely specified bases in nucleic acid sequences,
 30 Recommendations 1984., *Eur J Biochem.* 150(1):1-5 (1985).

| Symbol | Meaning | Group/Origin of Designation | Complementary Symbol |
|--------|---------|-----------------------------|----------------------|
| a | a | Adenine | t/u |
| g | g | Guanine | c |
| c | c | Cytosine | g |

| | | | |
|---|--|------------------------------|---|
| t | t | Thymine | a |
| u | u | Uracil | a |
| r | g or a | puRine | y |
| y | t/u or c | pYrimidine | r |
| m | a or c | aMino | k |
| k | g or t/u | Keto | m |
| s | g or c | Strong interactions 3H-bonds | w |
| w | a or t/u | Weak interactions 2H-bonds | s |
| b | g or c or t/u | not a | v |
| d | a or g or t/u | not c | h |
| h | a or c or t/u | not g | d |
| v | a or g or c | not t, not u | b |
| n | a or g or c or t/u, unknown, or other | aNy | n |

The nucleic acid molecules may be modified chemically or biochemically or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those of skill in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (*e.g.*, methyl phosphonates, phosphotriesters, phosphoramidates, carbamates, etc.), charged linkages (*e.g.*, phosphorothioates, phosphorodithioates, etc.), pendent moieties (*e.g.*, polypeptides), intercalators (*e.g.*, acridine, psoralen, etc.), chelators, alkylators, and modified linkages (*e.g.*, alpha anomeric nucleic acids, etc.) The term “nucleic acid molecule” also includes any topological conformation, including single-stranded, double-stranded, partially duplexed, triplexed, hairpinned, circular and padlocked conformations. Also included are synthetic molecules that mimic polynucleotides in their ability to bind to a designated sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule.

A “gene” is defined as a nucleic acid molecule that comprises a nucleic acid sequence that encodes a polypeptide and the expression control sequences that surround the nucleic acid sequence that encodes the polypeptide. For instance, a gene may comprise a promoter, one or more enhancers, a nucleic acid sequence that encodes a polypeptide, downstream regulatory sequences and, possibly, other nucleic acid sequences involved in regulation of the expression of an RNA. As is well known in the art, eukaryotic genes usually contain both exons and introns. The term “exon” refers to a nucleic acid sequence found in genomic DNA that is bioinformatically predicted and/or

experimentally confirmed to contribute contiguous sequence to a mature mRNA transcript. The term “intron” refers to a nucleic acid sequence found in genomic DNA that is predicted and/or confirmed to not contribute to a mature mRNA transcript, but rather to be “spliced out” during processing of the transcript.

5 A nucleic acid molecule or polypeptide is “derived” from a particular species if the nucleic acid molecule or polypeptide has been isolated from the particular species, or if the nucleic acid molecule or polypeptide is homologous to a nucleic acid molecule or polypeptide isolated from a particular species.

 An “isolated” or “substantially pure” nucleic acid or polynucleotide (*e.g.*, an RNA,
10 DNA or a mixed polymer) is one which is substantially separated from other cellular components that naturally accompany the native polynucleotide in its natural host cell, *e.g.*, ribosomes, polymerases, or genomic sequences with which it is naturally associated. The term embraces a nucleic acid or polynucleotide that (1) has been removed from its naturally occurring environment, (2) is not associated with all or a portion of a
15 polynucleotide in which the “isolated polynucleotide” is found in nature, (3) is operatively linked to a polynucleotide which it is not linked to in nature, (4) does not occur in nature as part of a larger sequence or (5) includes nucleotides or internucleoside bonds that are not found in nature. The term “isolated” or “substantially pure” also can be used in reference to recombinant or cloned DNA isolates, chemically synthesized polynucleotide
20 analogs, or polynucleotide analogs that are biologically synthesized by heterologous systems. The term “isolated nucleic acid molecule” includes nucleic acid molecules that are integrated into a host cell chromosome at a heterologous site, recombinant fusions of a native fragment to a heterologous sequence, recombinant vectors present as episomes or as integrated into a host cell chromosome.

25 A “part” of a nucleic acid molecule refers to a nucleic acid molecule that comprises a partial contiguous sequence of at least 10 bases of the reference nucleic acid molecule. Preferably, a part comprises at least 15 to 20 bases of a reference nucleic acid molecule. In theory, a nucleic acid sequence of 17 nucleotides is of sufficient length to occur at random less frequently than once in the three gigabase human genome, and thus
30 to provide a nucleic acid probe that can uniquely identify the reference sequence in a nucleic acid mixture of genomic complexity. A preferred part is one that comprises a nucleic acid sequence that can encode at least 6 contiguous amino acid sequences (fragments of at least 18 nucleotides) because they are useful in directing the expression or

synthesis of peptides that are useful in mapping the epitopes of the polypeptide encoded by the reference nucleic acid. *See, e.g., Geysen et al., Proc. Natl. Acad. Sci. USA* 81:3998-4002 (1984); and U.S. Patent Nos. 4,708,871 and 5,595,915, the disclosures of which are incorporated herein by reference in their entireties. A part may also comprise at least 25, 30, 35 or 40 nucleotides of a reference nucleic acid molecule, or at least 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400 or 500 nucleotides of a reference nucleic acid molecule. A part of a nucleic acid molecule may comprise no other nucleic acid sequences. Alternatively, a part of a nucleic acid may comprise other nucleic acid sequences from other nucleic acid molecules.

10 The term "oligonucleotide" refers to a nucleic acid molecule generally comprising a length of 200 bases or fewer. The term often refers to single-stranded deoxyribonucleotides, but it can refer as well to single-or double-stranded ribonucleotides, RNA:DNA hybrids and double-stranded DNAs, among others. Preferably, oligonucleotides are 10 to 60 bases in length and most preferably 12, 13, 14, 15, 16, 17, 18, 19 or 20 bases in length. Other preferred oligonucleotides are 25, 30, 35, 40, 45, 50, 55 or 60 bases in length. Oligonucleotides may be single-stranded, *e.g.* for use as probes or primers, or may be double-stranded, *e.g.* for use in the construction of a mutant gene. Oligonucleotides of the invention can be either sense or antisense oligonucleotides. An oligonucleotide can be derivatized or modified as discussed above for nucleic acid molecules.

Oligonucleotides, such as single-stranded DNA probe oligonucleotides, often are synthesized by chemical methods, such as those implemented on automated oligonucleotide synthesizers. However, oligonucleotides can be made by a variety of other methods, including in vitro recombinant DNA-mediated techniques and by expression of DNAs in cells and organisms. Initially, chemically synthesized DNAs typically are obtained without a 5' phosphate. The 5' ends of such oligonucleotides are not substrates for phosphodiester bond formation by ligation reactions that employ DNA ligases typically used to form recombinant DNA molecules. Where ligation of such oligonucleotides is desired, a phosphate can be added by standard techniques, such as those that employ a kinase and ATP. The 3' end of a chemically synthesized oligonucleotide generally has a free hydroxyl group and, in the presence of a ligase, such as T4 DNA ligase, readily will form a phosphodiester bond with a 5' phosphate of another polynucleotide, such as another oligonucleotide. As is well known, this reaction can be

prevented selectively, where desired, by removing the 5' phosphates of the other polynucleotide(s) prior to ligation.

The term "naturally occurring nucleotide" referred to herein includes naturally occurring deoxyribonucleotides and ribonucleotides. The term "modified nucleotides" referred to herein includes nucleotides with modified or substituted sugar groups and the like. The term "nucleotide linkages" referred to herein includes nucleotide linkages such as phosphorothioate, phosphorodithioate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phosphoraniladate, phosphoroamidate, and the like. *See e.g., LaPlanche et al. Nucl. Acids Res.* 14:9081-9093 (1986); *Stein et al. Nucl. Acids Res.* 16:3209-3221 (1988); *Zon et al. Anti-Cancer Drug Design* 6:539-568 (1991); *Zon et al., in Eckstein (ed.) Oligonucleotides and Analogues: A Practical Approach*, pp. 87-108, Oxford University Press (1991); *Uhlmann and Peyman Chemical Reviews* 90:543 (1990), and U.S. Patent No. 5,151,510, the disclosure of which is hereby incorporated by reference in its entirety.

Unless specified otherwise, the left hand end of a polynucleotide sequence in sense orientation is the 5' end and the right hand end of the sequence is the 3' end. In addition, the left hand direction of a polynucleotide sequence in sense orientation is referred to as the 5' direction, while the right hand direction of the polynucleotide sequence is referred to as the 3' direction. Further, unless otherwise indicated, each nucleotide sequence is set forth herein as a sequence of deoxyribonucleotides. It is intended, however, that the given sequence be interpreted as would be appropriate to the polynucleotide composition: for example, if the isolated nucleic acid is composed of RNA, the given sequence intends ribonucleotides, with uridine substituted for thymidine.

The term "allelic variant" refers to one of two or more alternative naturally occurring forms of a gene, wherein each gene possesses a unique nucleotide sequence. In a preferred embodiment, different alleles of a given gene have similar or identical biological properties.

The term "percent sequence identity" in the context of nucleic acid sequences refers to the residues in two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over a stretch of at least about nine nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 32 nucleotides, and preferably at least about 36 or more nucleotides. There are a number

of different algorithms known in the art which can be used to measure nucleotide sequence identity. For instance, polynucleotide sequences can be compared using FASTA, Gap or Bestfit, which are programs in Wisconsin Package Version 10.0, Genetics Computer Group (GCG), Madison, Wisconsin. FASTA, which includes, *e.g.*, the programs FASTA2
5 and FASTA3, provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson, *Methods Enzymol.* 183: 63-98 (1990); Pearson, *Methods Mol. Biol.* 132: 185-219 (2000); Pearson, *Methods Enzymol.* 266: 227-258 (1996); Pearson, *J. Mol. Biol.* 276: 71-84 (1998)). Unless otherwise specified, default parameters for a particular program or algorithm are used. For instance,
10 percent sequence identity between nucleic acid sequences can be determined using FASTA with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) or using Gap with its default parameters as provided in GCG Version 6.1.

A reference to a nucleic acid sequence encompasses its complement unless otherwise specified. Thus, a reference to a nucleic acid molecule having a particular
15 sequence should be understood to encompass its complementary strand, with its complementary sequence. The complementary strand is also useful, *e.g.*, for antisense therapy, double stranded RNA (dsRNA) inhibition (RNAi), combination of triplex and antisense, hybridization probes and PCR primers.

In the molecular biology art, researchers use the terms "percent sequence identity",
20 "percent sequence similarity" and "percent sequence homology" interchangeably. In this application, these terms shall have the same meaning with respect to nucleic acid sequences only.

The term "substantial similarity" or "substantial sequence similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with
25 appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 50%, more preferably 60% of the nucleotide bases, usually at least about 70%, more usually at least about 80%, preferably at least about 90%, and more preferably at least about 95-98% of the nucleotide bases, as measured by any well known algorithm of sequence identity, such
30 as FASTA, BLAST or Gap, as discussed above.

Alternatively, substantial similarity exists between a first and second nucleic acid sequence when the first nucleic acid sequence or fragment thereof hybridizes to an antisense strand of the second nucleic acid, under selective hybridization conditions.

Typically, selective hybridization will occur between the first nucleic acid sequence and an antisense strand of the second nucleic acid sequence when there is at least about 55% sequence identity between the first and second nucleic acid sequences— preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90% —
 5 over a stretch of at least about 14 nucleotides, more preferably at least 17 nucleotides, even more preferably at least 20, 25, 30, 35, 40, 50, 60, 70, 80, 90 or 100 nucleotides.

Nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, solvents, the base composition of the hybridizing species, length of the complementary regions, and the number of nucleotide base mismatches
 10 between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art. “Stringent hybridization conditions” and “stringent wash conditions” in the context of nucleic acid hybridization experiments depend upon a number of different physical parameters. The most important parameters include temperature of hybridization, base composition of the nucleic acids, salt concentration and length of the nucleic acid. One
 15 having ordinary skill in the art knows how to vary these parameters to achieve a particular stringency of hybridization. In general, “stringent hybridization” is performed at about 25°C below the thermal melting point (T_m) for the specific DNA hybrid under a particular set of conditions. “Stringent washing” is performed at temperatures about 5°C lower than the T_m for the specific DNA hybrid under a particular set of conditions. The T_m is the
 20 temperature at which 50% of the target sequence hybridizes to a perfectly matched probe. See Sambrook (1989), *supra*, p. 9.51.

The T_m for a particular DNA-DNA hybrid can be estimated by the formula:

$$T_m = 81.5^{\circ}\text{C} + 16.6 (\log_{10}[\text{Na}^+]) + 0.41 (\text{fraction G} + \text{C}) - 0.63 (\% \text{ formamide}) - (600/l) \text{ where } l \text{ is the length of the hybrid in base pairs.}$$

25 The T_m for a particular RNA-RNA hybrid can be estimated by the formula:

$$T_m = 79.8^{\circ}\text{C} + 18.5 (\log_{10}[\text{Na}^+]) + 0.58 (\text{fraction G} + \text{C}) + 11.8 (\text{fraction G} + \text{C})^2 - 0.35 (\% \text{ formamide}) - (820/l).$$

The T_m for a particular RNA-DNA hybrid can be estimated by the formula:

$$T_m = 79.8^{\circ}\text{C} + 18.5 (\log_{10}[\text{Na}^+]) + 0.58 (\text{fraction G} + \text{C}) + 11.8 (\text{fraction G} + \text{C})^2 - 0.50 (\% \text{ formamide}) - (820/l).$$

30 In general, the T_m decreases by 1-1.5°C for each 1% of mismatch between two nucleic acid sequences. Thus, one having ordinary skill in the art can alter hybridization and/or washing conditions to obtain sequences that have higher or lower degrees of

sequence identity to the target nucleic acid. For instance, to obtain hybridizing nucleic acids that contain up to 10% mismatch from the target nucleic acid sequence, 10-15°C would be subtracted from the calculated T_m of a perfectly matched hybrid, and then the hybridization and washing temperatures adjusted accordingly. Probe sequences may also
5 hybridize specifically to duplex DNA under certain conditions to form triplex or other higher order DNA complexes. The preparation of such probes and suitable hybridization conditions are well known in the art.

An example of stringent hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on
10 a filter in a Southern or Northern blot or for screening a library is 50% formamide/6X SSC at 42°C for at least ten hours and preferably overnight (approximately 16 hours). Another example of stringent hybridization conditions is 6X SSC at 68°C without formamide for at least ten hours and preferably overnight. An example of moderate stringency hybridization conditions is 6X SSC at 55°C without formamide for at least ten hours and
15 preferably overnight. An example of low stringency hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or northern blot or for screening a library is 6X SSC at 42°C for at least ten hours. Hybridization conditions to identify nucleic acid sequences that are similar but not identical can be identified by experimentally changing
20 the hybridization temperature from 68°C to 42°C while keeping the salt concentration constant (6X SSC), or keeping the hybridization temperature and salt concentration constant (e.g. 42°C and 6X SSC) and varying the formamide concentration from 50% to 0%. Hybridization buffers may also include blocking agents to lower background. These agents are well known in the art. *See Sambrook et al. (1989), supra*, pages 8.46 and 9.46-
25 9.58. *See also Ausubel (1992), supra, Ausubel (1999), supra, and Sambrook (2001), supra.*

Wash conditions also can be altered to change stringency conditions. An example of stringent wash conditions is a 0.2x SSC wash at 65°C for 15 minutes (*see Sambrook (1989), supra*, for SSC buffer). Often the high stringency wash is preceded by a low
30 stringency wash to remove excess probe. An exemplary medium stringency wash for duplex DNA of more than 100 base pairs is 1x SSC at 45°C for 15 minutes. An exemplary low stringency wash for such a duplex is 4x SSC at 40°C for 15 minutes. In

general, signal-to-noise ratio of 2x or higher than that observed for an unrelated probe in the particular hybridization assay indicates detection of a specific hybridization.

As defined herein, nucleic acids that do not hybridize to each other under stringent conditions are still substantially similar to one another if they encode polypeptides that are substantially identical to each other. This occurs, for example, when a nucleic acid is
5 created synthetically or recombinantly using a high codon degeneracy as permitted by the redundancy of the genetic code.

Hybridization conditions for nucleic acid molecules that are shorter than 100 nucleotides in length (*e.g.*, for oligonucleotide probes) may be calculated by the formula:

10 $T_m = 81.5^{\circ}\text{C} + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\text{fraction G+C}) - (600/N)$, wherein N is change length and the $[\text{Na}^+]$ is 1 M or less. *See* Sambrook (1989), *supra*, p. 11.46. For hybridization of probes shorter than 100 nucleotides, hybridization is usually performed under stringent conditions (5-10°C below the T_m) using high concentrations (0.1-1.0 pmol/ml) of probe. *Id.* at p. 11.45. Determination of hybridization using mismatched
15 probes, pools of degenerate probes or “guessmers,” as well as hybridization solutions and methods for empirically determining hybridization conditions are well known in the art. *See, e.g.*, Ausubel (1999), *supra*; Sambrook (1989), *supra*, pp. 11.45-11.57.

The term “digestion” or “digestion of DNA” refers to catalytic cleavage of the DNA with a restriction enzyme that acts only at certain sequences in the DNA. The
20 various restriction enzymes referred to herein are commercially available and their reaction conditions, cofactors and other requirements for use are known and routine to the skilled artisan. For analytical purposes, typically, 1 µg of plasmid or DNA fragment is digested with about 2 units of enzyme in about 20 µl of reaction buffer. For the purpose of isolating DNA fragments for plasmid construction, typically 5 to 50 µg of DNA are
25 digested with 20 to 250 units of enzyme in proportionately larger volumes. Appropriate buffers and substrate amounts for particular restriction enzymes are described in standard laboratory manuals, such as those referenced below, and are specified by commercial suppliers. Incubation times of about 1 hour at 37°C are ordinarily used, but conditions may vary in accordance with standard procedures, the supplier’s instructions and the
30 particulars of the reaction. After digestion, reactions may be analyzed, and fragments may be purified by electrophoresis through an agarose or polyacrylamide gel, using well known methods that are routine for those skilled in the art.

The term "ligation" refers to the process of forming phosphodiester bonds between two or more polynucleotides, which most often are double-stranded DNAs. Techniques for ligation are well known to the art and protocols for ligation are described in standard laboratory manuals and references, such as, *e.g.*, Sambrook (1989), *supra*.

5 Genome-derived "single exon probes," are probes that comprise at least part of an exon ("reference exon") and can hybridize detectably under high stringency conditions to transcript-derived nucleic acids that include the reference exon but do not hybridize detectably under high stringency conditions to nucleic acids that lack the reference exon. Single exon probes typically further comprise, contiguous to a first end of the exon
10 portion, a first intronic and/or intergenic sequence that is identically contiguous to the exon in the genome, and may contain a second intronic and/or intergenic sequence that is identically contiguous to the exon in the genome. The minimum length of genome-derived single exon probes is defined by the requirement that the exonic portion be of sufficient length to hybridize under high stringency conditions to transcript-derived
15 nucleic acids, as discussed above. The maximum length of genome-derived single exon probes is defined by the requirement that the probes contain portions of no more than one exon. The single exon probes may contain priming sequences not found in contiguity with the rest of the probe sequence in the genome, which priming sequences are useful for PCR and other amplification-based technologies. In another aspect, the invention is directed to
20 single exon probes based on the HSNAs disclosed herein.

In one embodiment, the term "microarray" refers to a "nucleic acid microarray" having a substrate-bound plurality of nucleic acids, hybridization to each of the plurality of bound nucleic acids being separately detectable. The substrate can be solid or porous, planar or non-planar, unitary or distributed. Nucleic acid microarrays include all the
25 devices so called in Schena (ed.), DNA Microarrays: A Practical Approach (Practical Approach Series), Oxford University Press (1999); *Nature Genet.* 21(1)(suppl.):1 - 60 (1999); Schena (ed.), Microarray Biochip: Tools and Technology, Eaton Publishing Company/BioTechniques Books Division (2000). Additionally, these nucleic acid microarrays include substrate-bound plurality of nucleic acids in which the plurality of
30 nucleic acids are disposed on a plurality of beads, rather than on a unitary planar substrate, as is described, *inter alia*, in Brenner *et al.*, *Proc. Natl. Acad. Sci. USA* 97(4):1665-1670 (2000). Examples of nucleic acid microarrays may be found in U.S. Patent Nos. 6,391,623, 6,383,754, 6,383,749, 6,380,377, 6,379,897, 6,376,191, 6,372,431, 6,351,712

6,344,316, 6,316,193, 6,312,906, 6,309,828, 6,309,824, 6,306,643, 6,300,063, 6,287,850, 6,284,497, 6,284,465, 6,280,954, 6,262,216, 6,251,601, 6,245,518, 6,263,287, 6,251,601, 6,238,866, 6,228,575, 6,214,587, 6,203,989, 6,171,797, 6,103,474, 6,083,726, 6,054,274, 6,040,138, 6,083,726, 6,004,755, 6,001,309, 5,958,342, 5,952,180, 5,936,731, 5,843,655, 5,814,454, 5,837,196, 5,436,327, 5,412,087, 5,405,783, the disclosures of which are incorporated herein by reference in their entireties.

In an alternative embodiment, a "microarray" may also refer to a "peptide microarray" or "protein microarray" having a substrate-bound collection of plurality of polypeptides, the binding to each of the plurality of bound polypeptides being separately detectable. Alternatively, the peptide microarray may have a plurality of binders, including but not limited to monoclonal antibodies, polyclonal antibodies, phage display binders, yeast 2 hybrid binders, aptamers, which can specifically detect the binding of the polypeptides of this invention. The array may be based on autoantibody detection to the polypeptides of this invention, see Robinson *et al.*, *Nature Medicine* 8(3):295-301 (2002). Examples of peptide arrays may be found in WO 02/31463, WO 02/25288, WO 01/94946, WO 01/88162, WO 01/68671, WO 01/57259, WO 00/61806, WO 00/54046, WO 00/47774, WO 99/40434, WO 99/39210, WO 97/42507 and U.S. Patent Nos. 6,268,210, 5,766,960, 5,143,854, the disclosures of which are incorporated herein by reference in their entireties.

In addition, determination of the levels of the HSNA or HSP may be made in a multiplex manner using techniques described in WO 02/29109, WO 02/24959, WO 01/83502, WO01/73113, WO 01/59432, WO 01/57269, WO 99/67641, the disclosures of which are incorporated herein by reference in their entireties.

The term "mutant", "mutated", or "mutation" when applied to nucleic acid sequences means that nucleotides in a nucleic acid sequence may be inserted, deleted or changed compared to a reference nucleic acid sequence. A single alteration may be made at a locus (a point mutation) or multiple nucleotides may be inserted, deleted or changed at a single locus. In addition, one or more alterations may be made at any number of loci within a nucleic acid sequence. In a preferred embodiment of the present invention, the nucleic acid sequence is the wild type nucleic acid sequence encoding a HSP or is a HSNA. The nucleic acid sequence may be mutated by any method known in the art including those mutagenesis techniques described *infra*.

The term “error-prone PCR” refers to a process for performing PCR under conditions where the copying fidelity of the DNA polymerase is low, such that a high rate of point mutations is obtained along the entire length of the PCR product. *See, e.g., Leung et al., Technique 1: 11-15 (1989) and Caldwell et al., PCR Methods Applic. 2: 28-33*

5 (1992).

The term “oligonucleotide-directed mutagenesis” refers to a process which enables the generation of site-specific mutations in any cloned DNA segment of interest. *See, e.g., Reidhaar-Olson et al., Science 241: 53-57 (1988).*

The term “assembly PCR” refers to a process which involves the assembly of a
10 PCR product from a mixture of small DNA fragments. A large number of different PCR reactions occur in parallel in the same vial, with the products of one reaction priming the products of another reaction.

The term “sexual PCR mutagenesis” or “DNA shuffling” refers to a method of error-prone PCR coupled with forced homologous recombination between DNA
15 molecules of different but highly related DNA sequence *in vitro*, caused by random fragmentation of the DNA molecule based on sequence similarity, followed by fixation of the crossover by primer extension in an error-prone PCR reaction. *See, e.g., Stemmer, Proc. Natl. Acad. Sci. U.S.A. 91: 10747-10751 (1994).* DNA shuffling can be carried out between several related genes (“Family shuffling”).

The term “*in vivo* mutagenesis” refers to a process of generating random mutations
20 in any cloned DNA of interest which involves the propagation of the DNA in a strain of bacteria such as *E. coli* that carries mutations in one or more of the DNA repair pathways. These “mutator” strains have a higher random mutation rate than that of a wild-type parent. Propagating the DNA in a mutator strain will eventually generate random
25 mutations within the DNA.

The term “cassette mutagenesis” refers to any process for replacing a small region of a double-stranded DNA molecule with a synthetic oligonucleotide “cassette” that differs from the native sequence. The oligonucleotide often contains completely and/or partially randomized native sequence.

30 The term “recursive ensemble mutagenesis” refers to an algorithm for protein engineering (protein mutagenesis) developed to produce diverse populations of phenotypically related mutants whose members differ in amino acid sequence. This

method uses a feedback mechanism to control successive rounds of combinatorial cassette mutagenesis. *See, e.g., Arkin et al., Proc. Natl. Acad. Sci. U.S.A.* 89: 7811-7815 (1992).

The term "exponential ensemble mutagenesis" refers to a process for generating combinatorial libraries with a high percentage of unique and functional mutants, wherein
5 small groups of residues are randomized in parallel to identify, at each altered position, amino acids which lead to functional proteins. *See, e.g., Delegrave et al., Biotechnology Research* 11: 1548-1552 (1993); Arnold, *Current Opinion in Biotechnology* 4: 450-455 (1993).

"Operatively linked" expression control sequences refers to a linkage in which the
10 expression control sequence is either contiguous with the gene of interest to control the gene of interest, or acts in *trans* or at a distance to control the gene of interest.

The term "expression control sequence" as used herein refers to polynucleotide sequences which are necessary to affect the expression of coding sequences to which they are operatively linked. Expression control sequences are sequences which control the
15 transcription, post-transcriptional events and translation of nucleic acid sequences. Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (*e.g.,* ribosome binding sites); sequences that enhance
20 protein stability; and when desired, sequences that enhance protein secretion. The nature of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence. The term "control sequences" is intended to include, at a minimum, all components whose presence is essential for expression, and can also include additional
25 components whose presence is advantageous, for example, leader sequences and fusion partner sequences.

The term "vector," as used herein, is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which
30 additional DNA segments may be ligated. Other vectors include cosmids, bacterial artificial chromosomes (BAC) and yeast artificial chromosomes (YAC). Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Viral vectors that infect bacterial cells are referred to as bacteriophages. Certain

vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication). Other vectors can be integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as “recombinant expression vectors” (or simply, “expression vectors”). In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, “plasmid” and “vector” may be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include other forms of expression vectors that serve equivalent functions.

The term “recombinant host cell” (or simply “host cell”), as used herein, is intended to refer to a cell into which a recombinant expression vector has been introduced. It should be understood that such terms are intended to refer not only to the particular subject cell but to the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term “host cell” as used herein.

As used herein, the phrase “open reading frame” and the equivalent acronym “ORF” refers to that portion of a transcript-derived nucleic acid that can be translated in its entirety into a sequence of contiguous amino acids. As so defined, an ORF has length, measured in nucleotides, exactly divisible by 3. As so defined, an ORF need not encode the entirety of a natural protein.

As used herein, the phrase “ORF-encoded peptide” refers to the predicted or actual translation of an ORF.

As used herein, the phrase “degenerate variant” of a reference nucleic acid sequence is meant to be inclusive of all nucleic acid sequences that can be directly translated, using the standard genetic code, to provide an amino acid sequence identical to that translated from the reference nucleic acid sequence.

The term “polypeptide” encompasses both naturally occurring and non-naturally occurring proteins and polypeptides, as well as polypeptide fragments and polypeptide mutants, derivatives and analogs thereof. A polypeptide may be monomeric or polymeric. Further, a polypeptide may comprise a number of different modules within a single

polypeptide each of which has one or more distinct activities. A preferred polypeptide in accordance with the invention comprises a HSP encoded by a nucleic acid molecule of the instant invention, or a fragment, mutant, analog and derivative thereof.

The term "isolated protein" or "isolated polypeptide" is a protein or polypeptide
5 that by virtue of its origin or source of derivation (1) is not associated with naturally associated components that accompany it in its native state, (2) is free of other proteins from the same species (3) is expressed by a cell from a different species, or (4) does not occur in nature. Thus, a polypeptide that is chemically synthesized or synthesized in a cellular system different from the cell from which it naturally originates will be "isolated"
10 from its naturally associated components. A polypeptide or protein may also be rendered substantially free of naturally associated components by isolation, using protein purification techniques well known in the art.

A protein or polypeptide is "substantially pure," "substantially homogeneous" or "substantially purified" when at least about 60% to 75% of a sample exhibits a single
15 species of polypeptide. The polypeptide or protein may be monomeric or multimeric. A substantially pure polypeptide or protein will typically comprise about 50%, 60%, 70%, 80% or 90% W/W of a protein sample, more usually about 95%, and preferably will be over 99% pure. Protein purity or homogeneity may be determined by a number of means well known in the art, such as polyacrylamide gel electrophoresis of a protein sample,
20 followed by visualizing a single polypeptide band upon staining the gel with a stain well known in the art. For certain purposes, higher resolution may be provided by using HPLC or other means well known in the art for purification.

The term "fragment" when used herein with respect to polypeptides of the present invention refers to a polypeptide that has an amino-terminal and/or carboxy-terminal
25 deletion compared to a full-length HSP. In a preferred embodiment, the fragment is a contiguous sequence in which the amino acid sequence of the fragment is identical to the corresponding positions in the naturally occurring polypeptide. Fragments typically are at least 5, 6, 7, 8, 9 or 10 amino acids long, preferably at least 12, 14, 16 or 18 amino acids long, more preferably at least 20 amino acids long, more preferably at least 25, 30, 35, 40
30 or 45, amino acids, even more preferably at least 50 or 60 amino acids long, and even more preferably at least 70 amino acids long.

A "derivative" when used herein with respect to polypeptides of the present invention refers to a polypeptide which is substantially similar in primary structural

sequence to a HSP but which include, *e.g.*, *in vivo* or *in vitro* chemical and biochemical modifications that are not found in the HSP. Such modifications include, for example, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. Other modification include, *e.g.*, labeling with radionuclides, and various enzymatic modifications, as will be readily appreciated by those skilled in the art. A variety of methods for labeling polypeptides and of substituents or labels useful for such purposes are well known in the art, and include radioactive isotopes such as ^{125}I , ^{32}P , ^{35}S , ^{14}C and ^3H , ligands which bind to labeled antiligands (*e.g.*, antibodies), fluorophores, chemiluminescent agents, enzymes, and antiligands which can serve as specific binding pair members for a labeled ligand. The choice of label depends on the sensitivity required, ease of conjugation with the primer, stability requirements, and available instrumentation. Methods for labeling polypeptides are well known in the art. *See* Ausubel (1992), *supra*; Ausubel (1999), *supra*.

The term "fusion protein" refers to polypeptides of the present invention coupled to a heterologous amino acid sequences. Fusion proteins are useful because they can be constructed to contain two or more desired functional elements from two or more different proteins. A fusion protein comprises at least 10 contiguous amino acids from a polypeptide of interest, more preferably at least 20 or 30 amino acids, even more preferably at least 40, 50 or 60 amino acids, yet more preferably at least 75, 100 or 125 amino acids. Fusion proteins can be produced recombinantly by constructing a nucleic acid sequence that encodes the polypeptide or a fragment thereof in frame with a nucleic acid sequence encoding a different protein or peptide and then expressing the fusion protein. Alternatively, a fusion protein can be produced chemically by crosslinking the polypeptide or a fragment thereof to another protein.

The term "analog" refers to both polypeptide analogs and non-peptide analogs. The term "polypeptide analog" as used herein refers to a polypeptide that is comprised of a segment of at least 25 amino acids that has substantial identity to a portion of an amino acid sequence but which contains non-natural amino acids or non-natural inter-residue bonds. In a preferred embodiment, the analog has the same or similar biological activity as the native polypeptide. Typically, polypeptide analogs comprise a conservative amino acid substitution (or insertion or deletion) with respect to the naturally occurring sequence. Analogs typically are at least 20 amino acids long, preferably at least 50 amino acids long or longer, and can often be as long as a full-length naturally occurring polypeptide.

The term "non-peptide analog" refers to a compound with properties that are analogous to those of a reference polypeptide. A non-peptide compound may also be termed a "peptide mimetic" or a "peptidomimetic." Such compounds are often developed with the aid of computerized molecular modeling. Peptide mimetics that are structurally similar to useful peptides may be used to produce an equivalent effect. Generally, peptidomimetics are structurally similar to a paradigm polypeptide (*i.e.*, a polypeptide that has a desired biochemical property or pharmacological activity), but have one or more peptide linkages optionally replaced by a linkage selected from the group consisting of: --CH₂NH--, --CH₂S--, --CH₂-CH₂--, --CH=CH--(cis and trans), --COCH₂--, --CH(OH)CH₂--, and --CH₂SO--, by methods well known in the art. Systematic substitution of one or more amino acids of a consensus sequence with a D-amino acid of the same type (*e.g.*, D-lysine in place of L-lysine) may also be used to generate more stable peptides. In addition, constrained peptides comprising a consensus sequence or a substantially identical consensus sequence variation may be generated by methods known in the art (Rizo *et al.*, *Ann. Rev. Biochem.* 61:387-418 (1992)). For example, one may add internal cysteine residues capable of forming intramolecular disulfide bridges which cyclize the peptide.

The term "mutant" or "mutein" when referring to a polypeptide of the present invention relates to an amino acid sequence containing substitutions, insertions or deletions of one or more amino acids compared to the amino acid sequence of a HSP. A mutein may have one or more amino acid point substitutions, in which a single amino acid at a position has been changed to another amino acid, one or more insertions and/or deletions, in which one or more amino acids are inserted or deleted, respectively, in the

sequence of the naturally occurring protein, and/or truncations of the amino acid sequence at either or both the amino or carboxy termini. Further, a mutein may have the same or different biological activity as the naturally occurring protein. For instance, a mutein may have an increased or decreased biological activity. A mutein has at least 50% sequence similarity to the wild type protein, preferred is 60% sequence similarity, more preferred is 70% sequence similarity. Even more preferred are muteins having 80%, 85% or 90% sequence similarity to a HSP. In an even more preferred embodiment, a mutein exhibits 95% sequence identity, even more preferably 97%, even more preferably 98% and even more preferably 99%. Sequence similarity may be measured by any common sequence analysis algorithm, such as GAP or BESTFIT or other variation Smith-Waterman alignment. *See*, T. F. Smith and M. S. Waterman, J. Mol. Biol. 147:195-197 (1981) and W.R. Pearson, Genomics 11:635-650 (1991).

Preferred amino acid substitutions are those which: (1) reduce susceptibility to proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinity or enzymatic activity, and (5) confer or modify other physicochemical or functional properties of such analogs. For example, single or multiple amino acid substitutions (preferably conservative amino acid substitutions) may be made in the naturally occurring sequence (preferably in the portion of the polypeptide outside the domain(s) forming intermolecular contacts. In a preferred embodiment, the amino acid substitutions are moderately conservative substitutions or conservative substitutions. In a more preferred embodiment, the amino acid substitutions are conservative substitutions. A conservative amino acid substitution should not substantially change the structural characteristics of the parent sequence (*e.g.*, a replacement amino acid should not tend to disrupt a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterizes the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in Creighton (ed.), Proteins, Structures and Molecular Principles, W. H. Freeman and Company (1984); Branden *et al.* (ed.), Introduction to Protein Structure, Garland Publishing (1991); Thornton *et al.*, *Nature* 354:105-106 (1991).

As used herein, the twenty conventional amino acids and their abbreviations follow conventional usage. *See* Golub *et al.* (eds.), Immunology - A Synthesis 2nd Ed., Sinauer Associates (1991). Stereoisomers (*e.g.*, D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as α -, α -disubstituted amino acids, N-alkyl amino acids,

and other unconventional amino acids may also be suitable components for polypeptides of the present invention. Examples of unconventional amino acids include:

4-hydroxyproline, γ -carboxyglutamate, ϵ -N,N,N-trimethyllysine, ϵ -N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine,

- 5 5-hydroxylysine, s-N-methylarginine, and other similar amino acids and imino acids (*e.g.*, 4-hydroxyproline). In the polypeptide notation used herein, the lefthand direction is the amino terminal direction and the right hand direction is the carboxy-terminal direction, in accordance with standard usage and convention.

- By "homology" or "homologous" when referring to a polypeptide of the present invention it is meant polypeptides from different organisms with a similar sequence to the encoded amino acid sequence of a HSP and a similar biological activity or function. Although two polypeptides are said to be "homologous," this does not imply that there is necessarily an evolutionary relationship between the polypeptides. Instead, the term "homologous" is defined to mean that the two polypeptides have similar amino acid sequences and similar biological activities or functions. In a preferred embodiment, a homologous polypeptide is one that exhibits 50% sequence similarity to HSP, preferred is 60% sequence similarity, more preferred is 70% sequence similarity. Even more preferred are homologous polypeptides that exhibit 80%, 85% or 90% sequence similarity to a HSP. In a yet more preferred embodiment, a homologous polypeptide exhibits 95%, 97%, 98% or 99% sequence similarity.

- When "sequence similarity" is used in reference to polypeptides, it is recognized that residue positions that are not identical often differ by conservative amino acid substitutions. In a preferred embodiment, a polypeptide that has "sequence similarity" comprises conservative or moderately conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (*e.g.*, charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well known to those of skill in the art. *See, e.g., Pearson, Methods Mol. Biol.* 24: 307-31 (1994).

For instance, the following six groups each contain amino acids that are conservative substitutions for one another:

- 1) Serine (S), Threonine (T);
- 2) Aspartic Acid (D), Glutamic Acid (E);
- 5 3) Asparagine (N), Glutamine (Q);
- 4) Arginine (R), Lysine (K);
- 5) Isoleucine (I), Leucine (L), Methionine (M), Alanine (A), Valine (V), and
- 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W).

Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet *et al.*, *Science* 256: 1443-45 (1992). A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

Sequence similarity for polypeptides, which is also referred to as sequence identity, is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG contains programs such as "Gap" and "Bestfit" which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild type protein and a mutein thereof. *See, e.g.*, GCG Version 6.1. Other programs include FASTA, discussed *supra*.

A preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially blastp or tblastn. *See, e.g.*, Altschul *et al.*, *J. Mol. Biol.* 215: 403-410 (1990); Altschul *et al.*, *Nucleic Acids Res.* 25:3389-402 (1997). Preferred parameters for blastp are:

| | |
|--------------------------|---------------|
| Expectation value: | 10 (default) |
| Filter: | seg (default) |
| Cost to open a gap: | 11 (default) |
| 30 Cost to extend a gap: | 1 (default) |
| Max. alignments: | 100 (default) |
| Word size: | 11 (default) |
| No. of descriptions: | 100 (default) |

Penalty Matrix: BLOSUM62

The length of polypeptide sequences compared for homology will generally be at least about 16 amino acid residues, usually at least about 20 residues, more usually at least about 24 residues, typically at least about 28 residues, and preferably more than about 35 residues. When searching a database containing sequences from a large number of different organisms, it is preferable to compare amino acid sequences.

Algorithms other than blastp for database searching using amino acid sequences are known in the art. For instance, polypeptide sequences can be compared using FASTA, a program in GCG Version 6.1. FASTA (*e.g.*, FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (1990), *supra*; Pearson (2000), *supra*. For example, percent sequence identity between amino acid sequences can be determined using FASTA with its default or recommended parameters (a word size of 2 and the PAM250 scoring matrix), as provided in GCG Version 6.1.

An “antibody” refers to an intact immunoglobulin, or to an antigen-binding portion thereof that competes with the intact antibody for specific binding to a molecular species, *e.g.*, a polypeptide of the instant invention. Antigen-binding portions may be produced by recombinant DNA techniques or by enzymatic or chemical cleavage of intact antibodies.

Antigen-binding portions include, *inter alia*, Fab, Fab', F(ab')₂, Fv, dAb, and

complementarity determining region (CDR) fragments, single-chain antibodies (scFv), chimeric antibodies, diabodies and polypeptides that contain at least a portion of an immunoglobulin that is sufficient to confer specific antigen binding to the polypeptide. A Fab fragment is a monovalent fragment consisting of the VL, VH, CL and CH1 domains; a F(ab')₂ fragment is a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consists of the VH and CH1 domains; a Fv fragment consists of the VL and VH domains of a single arm of an antibody; and a dAb fragment consists of a VH domain. *See, e.g., Ward et al., Nature* 341: 544-546 (1989).

By “bind specifically” and “specific binding” as used herein it is meant the ability of the antibody to bind to a first molecular species in preference to binding to other molecular species with which the antibody and first molecular species are admixed. An antibody is said specifically to “recognize” a first molecular species when it can bind specifically to that first molecular species.

A single-chain antibody (scFv) is an antibody in which VL and VH regions are paired to form a monovalent molecule via a synthetic linker that enables them to be made as a single protein chain. *See, e.g., Bird et al., Science* 242: 423-426 (1988); *Huston et al., Proc. Natl. Acad. Sci. USA* 85: 5879-5883 (1988). Diabodies are bivalent, bispecific
5 antibodies in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen binding sites. *See e.g., Holliger et al., Proc. Natl. Acad. Sci. USA* 90: 6444-6448 (1993); *Poljak et al., Structure* 2: 1121-1123 (1994). One or more CDRs
10 may be incorporated into a molecule either covalently or noncovalently to make it an immunoadhesin. An immunoadhesin may incorporate the CDR(s) as part of a larger polypeptide chain, may covalently link the CDR(s) to another polypeptide chain, or may incorporate the CDR(s) noncovalently. The CDRs permit the immunoadhesin to specifically bind to a particular antigen of interest. A chimeric antibody is an antibody
15 that contains one or more regions from one antibody and one or more regions from one or more other antibodies.

An antibody may have one or more binding sites. If there is more than one binding site, the binding sites may be identical to one another or may be different. For instance, a naturally occurring immunoglobulin has two identical binding sites, a single-chain
20 antibody or Fab fragment has one binding site, while a "bispecific" or "bifunctional" antibody has two different binding sites.

An "isolated antibody" is an antibody that (1) is not associated with naturally-associated components, including other naturally-associated antibodies, that accompany it in its native state, (2) is free of other proteins from the same species, (3) is expressed by a
25 cell from a different species, or (4) does not occur in nature. It is known that purified proteins, including purified antibodies, may be stabilized with non-naturally-associated components. The non-naturally-associated component may be a protein, such as albumin (*e.g., BSA*) or a chemical such as polyethylene glycol (PEG).

A "neutralizing antibody" or "an inhibitory antibody" is an antibody that inhibits
30 the activity of a polypeptide or blocks the binding of a polypeptide to a ligand that normally binds to it. An "activating antibody" is an antibody that increases the activity of a polypeptide.

The term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or T-cell receptor. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three-dimensional structural characteristics, as well as specific charge characteristics. An antibody is said to specifically bind an antigen when the dissociation constant is less than $1\ \mu\text{M}$, preferably less than $100\ \text{nM}$ and most preferably less than $10\ \text{nM}$.

The term "patient" includes human and veterinary subjects.

Throughout this specification and claims, the word "comprise," or variations such as "comprises" or "comprising," will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

The term "hepatic specific" refers to a nucleic acid molecule or polypeptide that is expressed predominantly in the hepatic as compared to other tissues in the body. In a preferred embodiment, a "hepatic specific" nucleic acid molecule or polypeptide is detected at a level that is 1.5-fold higher than any other tissue in the body. In a more preferred embodiment, the "hepatic specific" nucleic acid molecule or polypeptide is detected at a level that is 2-fold higher than any other tissue in the body, more preferably 5-fold higher, still more preferably at least 10-fold, 15-fold, 20-fold, 25-fold, 50-fold or 100-fold higher than any other tissue in the body. Nucleic acid molecule levels may be measured by nucleic acid hybridization, such as Northern blot hybridization, or quantitative PCR. Polypeptide levels may be measured by any method known to accurately quantitate protein levels, such as Western blot analysis.

Nucleic Acid Molecules, Regulatory Sequences, Vectors, Host Cells and Recombinant Methods of Making Polypeptides

Nucleic Acid Molecules

One aspect of the invention provides isolated nucleic acid molecules that are specific to the hepatic or to hepatic cells or tissue or that are derived from such nucleic acid molecules. These isolated hepatic specific nucleic acids (HSNAs) may comprise cDNA genomic DNA, RNA, or a combination thereof, a fragment of one of these nucleic acids, or may be a non-naturally occurring nucleic acid molecule. A HSNA may be derived from an animal. In a preferred embodiment, the HSNA is derived from a human or other mammal. In a more preferred embodiment, the HSNA is derived from a human

or other primate. In an even more preferred embodiment, the HSNA is derived from a human.

In a preferred embodiment, the nucleic acid molecule encodes a polypeptide that is specific to hepatic, a hepatic-specific polypeptide (HSP). In a more preferred
5 embodiment, the nucleic acid molecule encodes a polypeptide that comprises an amino acid sequence of SEQ ID NO: 410-611. In another highly preferred embodiment, the nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1-409.

Nucleotide sequences of the instantly-described nucleic acid molecules were determined by assembling several DNA molecules from either public or proprietary databases. Some
10 of the underlying DNA sequences are the result, directly or indirectly, of at least one enzymatic polymerization reaction (*e.g.*, reverse transcription and/or polymerase chain reaction) using an automated sequencer (such as the MegaBACE™ 1000, Amersham Biosciences, Sunnyvale, CA, USA).

Nucleic acid molecules of the present invention may also comprise sequences that
15 selectively hybridizes to a nucleic acid molecule encoding a HSNA or a complement or antisense thereof. The hybridizing nucleic acid molecule may or may not encode a polypeptide or may or may not encode a HSP. However, in a preferred embodiment, the hybridizing nucleic acid molecule encodes a HSP. In a more preferred embodiment, the invention provides a nucleic acid molecule that selectively hybridizes to a nucleic acid
20 molecule or the antisense sequence of a nucleic acid molecule that encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 410-611. In an even more preferred embodiment, the invention provides a nucleic acid molecule that selectively hybridizes to a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1-409 or the antisense sequence thereof. Preferably, the nucleic acid molecule selectively hybridizes to
25 a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a HSP under low stringency conditions. More preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a HSP under moderate stringency conditions. Most preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense
30 sequence of a nucleic acid molecule encoding a HSP under high stringency conditions. In a preferred embodiment, the nucleic acid molecule hybridizes under low, moderate or high stringency conditions to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence of SEQ ID NO:

410-611. In a more preferred embodiment, the nucleic acid molecule hybridizes under low, moderate or high stringency conditions to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule comprising a nucleic acid sequence selected from SEQ ID NO: 1-409.

5 Nucleic acid molecules of the present invention may also comprise nucleic acid sequences that exhibit substantial sequence similarity to a nucleic acid encoding a HSP or a complement of the encoding nucleic acid molecule. In this embodiment, it is preferred that the nucleic acid molecule exhibit substantial sequence similarity to a nucleic acid molecule encoding human HSP. More preferred is a nucleic acid molecule exhibiting
10 substantial sequence similarity to a nucleic acid molecule encoding a polypeptide having an amino acid sequence of SEQ ID NO: 410-611. By substantial sequence similarity it is meant a nucleic acid molecule having at least 60% sequence identity with a nucleic acid molecule encoding a HSP, such as a polypeptide having an amino acid sequence of SEQ ID NO: 410-611, more preferably at least 70%, even more preferably at least 80% and
15 even more preferably at least 85%. In a more preferred embodiment, the similar nucleic acid molecule is one that has at least 90% sequence identity with a nucleic acid molecule encoding a HSP, more preferably at least 95%, more preferably at least 97%, even more preferably at least 98%, and still more preferably at least 99%. Most preferred in this embodiment is a nucleic acid molecule that has at least 99.5%, 99.6%, 99.7%, 99.8% or
20 99.9% sequence identity with a nucleic acid molecule encoding a HSP.

 The nucleic acid molecules of the present invention are also inclusive of those exhibiting substantial sequence similarity to a HSNA or its complement. In this embodiment, it is preferred that the nucleic acid molecule exhibit substantial sequence similarity to a nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1-
25 409. By substantial sequence similarity it is meant a nucleic acid molecule that has at least 60% sequence identity with a HSNA, such as one having a nucleic acid sequence of SEQ ID NO: 1-409, more preferably at least 70%, even more preferably at least 80% and even more preferably at least 85%. More preferred is a nucleic acid molecule that has at least 90% sequence identity with a HSNA, more preferably at least 95%, more preferably
30 at least 97%, even more preferably at least 98%, and still more preferably at least 99%. Most preferred is a nucleic acid molecule that has at least 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity with a HSNA.

Nucleic acid molecules that exhibit substantial sequence similarity are inclusive of sequences that exhibit sequence identity over their entire length to a HSNA or to a nucleic acid molecule encoding a HSP, as well as sequences that are similar over only a part of its length. In this case, the part is at least 50 nucleotides of the HSNA or the nucleic acid molecule encoding a HSP, preferably at least 100 nucleotides, more preferably at least 150 or 200 nucleotides, even more preferably at least 250 or 300 nucleotides, still more preferably at least 400 or 500 nucleotides.

The substantially similar nucleic acid molecule may be a naturally occurring one that is derived from another species, especially one derived from another primate, wherein the similar nucleic acid molecule encodes an amino acid sequence that exhibits significant sequence identity to that of SEQ ID NO: 410-611 or demonstrates significant sequence identity to the nucleotide sequence of SEQ ID NO: 1-409. The similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule from a human, when the HSNA is a member of a gene family. The similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule derived from a non-primate, mammalian species, including without limitation, domesticated species, *e.g.*, dog, cat, mouse, rat, rabbit, hamster, cow, horse and pig; and wild animals, *e.g.*, monkey, fox, lions, tigers, bears, giraffes, zebras, etc. The substantially similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule derived from a non-mammalian species, such as birds or reptiles. The naturally occurring substantially similar nucleic acid molecule may be isolated directly from humans or other species. In another embodiment, the substantially similar nucleic acid molecule may be one that is experimentally produced by random mutation of a nucleic acid molecule. In another embodiment, the substantially similar nucleic acid molecule may be one that is experimentally produced by directed mutation of a HSNA. In a preferred embodiment, the substantially similar nucleic acid molecule is an HSNA.

The nucleic acid molecules of the present invention are also inclusive of allelic variants of a HSNA or a nucleic acid encoding a HSP. For example, single nucleotide polymorphisms (SNPs) occur frequently in eukaryotic genomes and the sequence determined from one individual of a species may differ from other allelic forms present within the population. More than 1.4 million SNPs have already identified in the human genome, International Human Genome Sequencing Consortium, *Nature* 409: 860-921 (2001) – Variants with small deletions and insertions of more than a single nucleotide are

also found in the general population, and often do not alter the function of the protein. In addition, amino acid substitutions occur frequently among natural allelic variants, and often do not substantially change protein function.

In a preferred embodiment, the allelic variant is a variant of a gene, wherein the gene is transcribed into an mRNA that encodes a HSP. In a more preferred embodiment, the gene is transcribed into an mRNA that encodes a HSP comprising an amino acid sequence of SEQ ID NO: 410-611. In another preferred embodiment, the allelic variant is a variant of a gene, wherein the gene is transcribed into an mRNA that is a HSNA. In a more preferred embodiment, the gene is transcribed into an mRNA that comprises the nucleic acid sequence of SEQ ID NO: 1-409. Also preferred is that the allelic variant is a naturally occurring allelic variant in the species of interest, particularly human.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences comprising a part of a nucleic acid sequence of the instant invention. The part may or may not encode a polypeptide, and may or may not encode a polypeptide that is a HSP. In a preferred embodiment, the part encodes a HSP. In one embodiment, the nucleic acid molecule comprises a part of a HSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that hybridizes or exhibits substantial sequence similarity to a HSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that is an allelic variant of a HSNA. In yet another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that encodes a HSP. A part comprises at least 10 nucleotides, more preferably at least 15, 17, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400 or 500 nucleotides. The maximum size of a nucleic acid part is one nucleotide shorter than the sequence of the nucleic acid molecule encoding the full-length protein.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences that encode fusion proteins, homologous proteins, polypeptide fragments, muteins and polypeptide analogs, as described *infra*.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences containing modifications of the native nucleic acid molecule. Examples of such modifications include, but are not limited to, nonnative internucleoside bonds, post-synthetic modifications or altered nucleotide analogues. One having ordinary skill in the art would recognize that the type of modification that may be made will depend upon the intended use of the nucleic acid molecule. For instance, when the nucleic acid molecule is

used as a hybridization probe, the range of such modifications will be limited to those that permit sequence-discriminating base pairing of the resulting nucleic acid. When used to direct expression of RNA or protein *in vitro* or *in vivo*, the range of such modifications will be limited to those that permit the nucleic acid to function properly as a polymerization substrate. When the isolated nucleic acid is used as a therapeutic agent, the modifications will be limited to those that do not confer toxicity upon the isolated nucleic acid.

Accordingly, in one embodiment, a nucleic acid molecule may include nucleotide analogues that incorporate labels that are directly detectable, such as radiolabels or fluorophores, or nucleotide analogues that incorporate labels that can be visualized in a subsequent reaction, such as biotin or various haptens. The labeled nucleic acid molecules are particularly useful as hybridization probes.

Common radiolabeled analogues include those labeled with ^{33}P , ^{32}P , and ^{35}S , such as α - ^{32}P -dATP, α - ^{32}P -dCTP, α - ^{32}P -dGTP, α - ^{32}P -dTTP, α - ^{32}P -3'dATP, α - ^{32}P -ATP, α - ^{32}P -CTP, α - ^{32}P -GTP, α - ^{32}P -UTP, α - ^{35}S -dATP, γ - ^{35}S -GTP, γ - ^{33}P -dATP, and the like.

Commercially available fluorescent nucleotide analogues readily incorporated into the nucleic acids of the present invention include Cy3-dCTP, Cy3-dUTP, Cy5-dCTP, Cy3-dUTP (Amersham Biosciences, Piscataway, New Jersey, USA), fluorescein-12-dUTP, tetramethylrhodamine-6-dUTP, Texas Red®-5-dUTP, Cascade Blue®-7-dUTP, BODIPY® FL-14-dUTP, BODIPY® TMR-14-dUTP, BODIPY® TR-14-dUTP, Rhodamine Green™-5-dUTP, Oregon Green® 488-5-dUTP, Texas Red®-12-dUTP, BODIPY® 630/650-14-dUTP, BODIPY® 650/665-14-dUTP, Alexa Fluor® 488-5-dUTP, Alexa Fluor® 532-5-dUTP, Alexa Fluor® 568-5-dUTP, Alexa Fluor® 594-5-dUTP, Alexa Fluor® 546-14-dUTP, fluorescein-12-UTP, tetramethylrhodamine-6-UTP, Texas Red®-5-UTP, Cascade Blue®-7-UTP, BODIPY® FL-14-UTP, BODIPY® TMR-14-UTP, BODIPY® TR-14-UTP, Rhodamine Green™-5-UTP, Alexa Fluor® 488-5-UTP, Alexa Fluor® 546-14-UTP (Molecular Probes, Inc. Eugene, OR, USA). One may also custom synthesize nucleotides having other fluorophores. See Henegariu *et al.*, *Nature Biotechnol.* 18: 345-348 (2000).

Haptens that are commonly conjugated to nucleotides for subsequent labeling include biotin (biotin-11-dUTP, Molecular Probes, Inc., Eugene, OR, USA; biotin-21-UTP, biotin-21-dUTP, Clontech Laboratories, Inc., Palo Alto, CA, USA), digoxigenin (DIG-11-dUTP, alkali labile, DIG-11-UTP, Roche Diagnostics Corp.,

Indianapolis, IN, USA), and dinitrophenyl (dinitrophenyl-11-dUTP, Molecular Probes, Inc., Eugene, OR, USA).

Nucleic acid molecules of the present invention can be labeled by incorporation of labeled nucleotide analogues into the nucleic acid. Such analogues can be incorporated by enzymatic polymerization, such as by nick translation, random priming, polymerase chain reaction (PCR), terminal transferase tailing, and end-filling of overhangs, for DNA molecules, and *in vitro* transcription driven, *e.g.*, from phage promoters, such as T7, T3, and SP6, for RNA molecules. Commercial kits are readily available for each such labeling approach. Analogues can also be incorporated during automated solid phase chemical synthesis. Labels can also be incorporated after nucleic acid synthesis, with the 5' phosphate and 3' hydroxyl providing convenient sites for post-synthetic covalent attachment of detectable labels.

Other post-synthetic approaches also permit internal labeling of nucleic acids. For example, fluorophores can be attached using a cisplatin reagent that reacts with the N7 of guanine residues (and, to a lesser extent, adenine bases) in DNA, RNA, and Peptide Nucleic Acids (PNA) to provide a stable coordination complex between the nucleic acid and fluorophore label (Universal Linkage System) (available from Molecular Probes, Inc., Eugene, OR, USA and Amersham Pharmacia Biotech, Piscataway, NJ, USA); *see Alers et al., Genes, Chromosomes & Cancer* 25: 301- 305 (1999); Jelsma *et al., J. NIH Res.* 5: 82 (1994); Van Belkum *et al., BioTechniques* 16: 148-153 (1994). Alternatively, nucleic acids can be labeled using a disulfide-containing linker (FastTag™ Reagent, Vector Laboratories, Inc., Burlingame, CA, USA) that is photo- or thermally coupled to the target nucleic acid using aryl azide chemistry; after reduction, a free thiol is available for coupling to a hapten, fluorophore, sugar, affinity ligand, or other marker.

One or more independent or interacting labels can be incorporated into the nucleic acid molecules of the present invention. For example, both a fluorophore and a moiety that in proximity thereto acts to quench fluorescence can be included to report specific hybridization through release of fluorescence quenching or to report exonucleotidic excision. *See, e.g., Tyagi et al., Nature Biotechnol.* 14: 303-308 (1996); Tyagi *et al., Nature Biotechnol.* 16: 49-53 (1998); Sokol *et al., Proc. Natl. Acad. Sci. USA* 95: 11538-11543 (1998); Kostrikis *et al., Science* 279: 1228-1229 (1998); Marras *et al., Genet. Anal.* 14: 151-156 (1999); Holland *et al., Proc. Natl. Acad. Sci. USA* 88: 7276-7280 (1991); Heid *et al., Genome Res.* 6(10): 986-94 (1996); Kuimelis *et al.,*

Nucleic Acids Symp. Ser. (37): 255-6 (1997); and U.S. Patent Nos. 5,846,726, 5,925,517, 5,925,517, 5,723,591 and 5,538,848, the disclosures of which are incorporated herein by reference in their entirety.

Nucleic acid molecules of the present invention may also be modified by altering
5 one or more native phosphodiester internucleoside bonds to more nuclease-resistant,
internucleoside bonds. See Hartmann *et al.* (eds.), Manual of Antisense Methodology:
Perspectives in Antisense Science, Kluwer Law International (1999); Stein *et al.* (eds.),
Applied Antisense Oligonucleotide Technology, Wiley-Liss (1998); Chadwick *et al.*
(eds.), Oligonucleotides as Therapeutic Agents – Symposium No. 209, John Wiley & Son
10 Ltd (1997). Such altered internucleoside bonds are often desired for techniques or for
targeted gene correction, Gamper *et al.*, *Nucl. Acids Res.* 28(21): 4332-4339 (2000). For
double stranded RNA inhibition which may utilize either natural ds RNA or ds RNA
modified in its, sugar, phosphate or base, see Hannon, *Nature* 418(11): 244-251 (2002);
Fire *et al.* in WO 99/32619; Tuschl *et al.* in US2002/0086356; Kruetzer *et al.* in WO
15 00/44895, the disclosures of which are incorporated herein by reference in their entirety;.
For circular antisense, see Kool in U.S. Patent No. 5,426,180, the disclosure of which is
incorporated herein by reference in its entirety.

Modified oligonucleotide backbones include, without limitation,
phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters,
20 aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'-alkylene
phosphonates and chiral phosphonates, phosphinates, phosphoramidates including
3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates,
thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having
normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity
25 wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'.
Representative U.S. Patents that teach the preparation of the above phosphorus-containing
linkages include, but are not limited to, U.S. Patent Nos. 3,687,808; 4,469,863; 4,476,301;
5,023,243; 5,177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131;
5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821;
30 5,541,306; 5,550,111; 5,563,253; 5,571,799; 5,587,361; and 5,625,050, the disclosures of
which are incorporated herein by reference in their entirety. In a preferred embodiment,
the modified internucleoside linkages may be used for antisense techniques.

Other modified oligonucleotide backbones do not include a phosphorus atom, but have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH₂ component parts. Representative U.S. patents that teach the preparation of the above backbones include, but are not limited to, U.S. Patent Nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437 and 5,677,439; the disclosures of which are incorporated herein by reference in their entireties.

In other preferred nucleic acid molecules, both the sugar and the internucleoside linkage are replaced with novel groups, such as peptide nucleic acids (PNA). In PNA compounds, the phosphodiester backbone of the nucleic acid is replaced with an amide-containing backbone, in particular by repeating N-(2-aminoethyl) glycine units linked by amide bonds. Nucleobases are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone, typically by methylene carbonyl linkages. PNA can be synthesized using a modified peptide synthesis protocol. PNA oligomers can be synthesized by both Fmoc and tBoc methods. Representative U.S. patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Patent Nos. 5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference in its entirety. Automated PNA synthesis is readily achievable on commercial synthesizers (*see, e.g.*, "PNA User's Guide," Rev. 2, February 1998, Perseptive Biosystems Part No. 60138, Applied Biosystems, Inc., Foster City, CA). PNA molecules are advantageous for a number of reasons. First, because the PNA backbone is uncharged, PNA/DNA and PNA/RNA duplexes have a higher thermal stability than is found in DNA/DNA and DNA/RNA duplexes. The T_m of a PNA/DNA or PNA/RNA duplex is generally 1°C higher per base pair than the T_m of the corresponding DNA/DNA or DNA/RNA duplex

(in 100 mM NaCl). Second, PNA molecules can also form stable PNA/DNA complexes at low ionic strength, under conditions in which DNA/DNA duplex formation does not occur. Third, PNA also demonstrates greater specificity in binding to complementary DNA because a PNA/DNA mismatch is more destabilizing than DNA/DNA mismatch. A
5 single mismatch in mixed a PNA/DNA 15-mer lowers the T_m by 8–20°C (15°C on average). In the corresponding DNA/DNA duplexes, a single mismatch lowers the T_m by 4–16°C (11°C on average). Because PNA probes can be significantly shorter than DNA probes, their specificity is greater. Fourth, PNA oligomers are resistant to degradation by enzymes, and the lifetime of these compounds is extended both *in vivo* and *in vitro*
10 because nucleases and proteases do not recognize the PNA polyamide backbone with nucleobase sidechains. See, e.g., Ray *et al.*, *FASEB J.* 14(9): 1041-60 (2000); Nielsen *et al.*, *Pharmacol Toxicol.* 86(1): 3-7 (2000); Larsen *et al.*, *Biochim Biophys Acta.* 1489(1): 159-66 (1999); Nielsen, *Curr. Opin. Struct. Biol.* 9(3): 353-7 (1999), and Nielsen, *Curr. Opin. Biotechnol.* 10(1): 71-5 (1999).

15 Nucleic acid molecules may be modified compared to their native structure throughout the length of the nucleic acid molecule or can be localized to discrete portions thereof. As an example of the latter, chimeric nucleic acids can be synthesized that have discrete DNA and RNA domains and that can be used for targeted gene repair and modified PCR reactions, as further described in, Misra *et al.*, *Biochem.* 37: 1917-1925
20 (1998); and Finn *et al.*, *Nucl. Acids Res.* 24: 3357-3363 (1996), and U.S. Patent Nos. 5,760,012 and 5,731,181, the disclosures of which are incorporated herein by reference in their entireties.

Unless otherwise specified, nucleic acid molecules of the present invention can include any topological conformation appropriate to the desired use; the term thus
25 explicitly comprehends, among others, single-stranded, double-stranded, triplexed, quadruplexed, partially double-stranded, partially-triplexed, partially-quadruplexed, branched, hairpinned, circular, and padlocked conformations. Padlock conformations and their utilities are further described in Banér *et al.*, *Curr. Opin. Biotechnol.* 12: 11-15
(2001); Escude *et al.*, *Proc. Natl. Acad. Sci. USA* 14: 96(19):10603-7 (1999); and Nilsson
30 *et al.*, *Science* 265(5181): 2085-8 (1994). Triplex and quadruplex conformations, and their utilities, are reviewed in Praseuth *et al.*, *Biochim. Biophys. Acta.* 1489(1): 181-206 (1999); Fox, *Curr. Med. Chem.* 7(1): 17-37 (2000); Kochetkova *et al.*, *Methods Mol. Biol.*

130: 189-201 (2000); Chan *et al.*, *J. Mol. Med.* 75(4): 267-82 (1997); Rowley *et al.*, *Mol Med* 5(10): 693-700 (1999); Kool, *Annu Rev Biophys Biomol Struct.* 25: 1-28 (1996).

Methods for Using Nucleic Acid Molecules as Probes and Primers

5 The isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize, and quantify hybridizing nucleic acids in, and isolate hybridizing nucleic acids from, both genomic and transcript-derived nucleic acid samples. When free in solution, such probes are typically, but not invariably, detectably labeled; bound to a substrate, as in a microarray, such probes are typically, but not
10 invariably unlabeled.

 In one embodiment, the isolated nucleic acid molecules of the present invention can be used as probes to detect and characterize gross alterations in the gene of a HSNA, such as deletions, insertions, translocations, and duplications of the HSNA genomic locus through fluorescence *in situ* hybridization (FISH) to chromosome spreads. *See, e.g.*,
15 Andreeff *et al.* (eds.), Introduction to Fluorescence In Situ Hybridization: Principles and Clinical Applications, John Wiley & Sons (1999). The isolated nucleic acid molecules of the present invention can be used as probes to assess smaller genomic alterations using, *e.g.*, Southern blot detection of restriction fragment length polymorphisms. The isolated nucleic acid molecules of the present invention can be used as probes to isolate genomic
20 clones that include a nucleic acid molecule of the present invention, which thereafter can be restriction mapped and sequenced to identify deletions, insertions, translocations, and substitutions (single nucleotide polymorphisms, SNPs) at the sequence level. Alternatively, detection techniques such as molecular beacons may be used, see Kostrikis *et al. Science* 279:1228-1229 (1998).

25 The isolated nucleic acid molecules of the present invention can be also be used as probes to detect, characterize, and quantify HSNA in, and isolate HSNA from, transcript-derived nucleic acid samples. In one embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize by length, and quantify mRNA by Northern blot of total or poly-A⁺- selected RNA samples. In
30 another embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize by location, and quantify mRNA by *in situ* hybridization to tissue sections. *See, e.g.*, Schwarchzacher *et al.*, In Situ Hybridization, Springer-Verlag New York (2000). In another preferred embodiment, the

isolated nucleic acid molecules of the present invention can be used as hybridization probes to measure the representation of clones in a cDNA library or to isolate hybridizing nucleic acid molecules acids from cDNA libraries, permitting sequence level characterization of mRNAs that hybridize to HSNA, including, without limitations, identification of deletions, insertions, substitutions, truncations, alternatively spliced forms and single nucleotide polymorphisms. In yet another preferred embodiment, the nucleic acid molecules of the instant invention may be used in microarrays.

All of the aforementioned probe techniques are well within the skill in the art, and are described at greater length in standard texts such as Sambrook (2001), *supra*; Ausubel (1999), *supra*; and Walker *et al.* (eds.), The Nucleic Acids Protocols Handbook, Humana Press (2000).

In another embodiment, a nucleic acid molecule of the invention may be used as a probe or primer to identify and/or amplify a second nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of the invention. In this embodiment, it is preferred that the probe or primer be derived from a nucleic acid molecule encoding a HSP. More preferably, the probe or primer is derived from a nucleic acid molecule encoding a polypeptide having an amino acid sequence of SEQ ID NO: 410-611. Also preferred are probes or primers derived from a HSNA. More preferred are probes or primers derived from a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-409.

In general, a probe or primer is at least 10 nucleotides in length, more preferably at least 12, more preferably at least 14 and even more preferably at least 16 or 17 nucleotides in length. In an even more preferred embodiment, the probe or primer is at least 18 nucleotides in length, even more preferably at least 20 nucleotides and even more preferably at least 22 nucleotides in length. Primers and probes may also be longer in length. For instance, a probe or primer may be 25 nucleotides in length, or may be 30, 40 or 50 nucleotides in length. Methods of performing nucleic acid hybridization using oligonucleotide probes are well known in the art. *See, e.g.*, Sambrook *et al.*, 1989, *supra*, Chapter 11 and pp. 11.31-11.32 and 11.40-11.44, which describes radiolabeling of short probes, and pp. 11.45-11.53, which describe hybridization conditions for oligonucleotide probes, including specific conditions for probe hybridization (pp. 11.50-11.51).

Methods of performing primer-directed amplification are also well known in the art. Methods for performing the polymerase chain reaction (PCR) are compiled, *inter alia*,

in McPherson, PCR Basics: From Background to Bench, Springer Verlag (2000); Innis *et al.* (eds.), PCR Applications: Protocols for Functional Genomics, Academic Press (1999); Gelfand *et al.* (eds.), PCR Strategies, Academic Press (1998); Newton *et al.*, PCR, Springer-Verlag New York (1997); Burke (ed.), PCR: Essential Techniques, John Wiley & Son Ltd (1996); White (ed.), PCR Cloning Protocols: From Molecular Cloning to Genetic Engineering, Vol. 67, Humana Press (1996); and McPherson *et al.* (eds.), PCR 2: A Practical Approach, Oxford University Press, Inc. (1995). Methods for performing RT-PCR are collected, *e.g.*, in Siebert *et al.* (eds.), Gene Cloning and Analysis by RT-PCR, Eaton Publishing Company/Bio Techniques Books Division, 1998; and Siebert (ed.), PCR Technique: RT-PCR, Eaton Publishing Company/ BioTechniques Books (1995).

PCR and hybridization methods may be used to identify and/or isolate nucleic acid molecules of the present invention including allelic variants, homologous nucleic acid molecules and fragments. PCR and hybridization methods may also be used to identify, amplify and/or isolate nucleic acid molecules of the present invention that encode homologous proteins, analogs, fusion protein or muteins of the invention. Nucleic acid primers as described herein can be used to prime amplification of nucleic acid molecules of the invention, using transcript-derived or genomic DNA as template.

These nucleic acid primers can also be used, for example, to prime single base extension (SBE) for SNP detection (*See, e.g.*, U.S. Pat. No. 6,004,744, the disclosure of which is incorporated herein by reference in its entirety).

Isothermal amplification approaches, such as rolling circle amplification, are also now well-described. *See, e.g.*, Schweitzer *et al.*, *Curr. Opin. Biotechnol.* 12(1): 21-7 (2001); international patent publications WO 97/19193 and WO 00/15779, and U.S. Patent Nos. 5,854,033 and 5,714,320, the disclosures of which are incorporated herein by reference in their entireties. Rolling circle amplification can be combined with other techniques to facilitate SNP detection. *See, e.g.*, Lizardi *et al.*, *Nature Genet.* 19(3): 225-32 (1998).

Nucleic acid molecules of the present invention may be bound to a substrate either covalently or noncovalently. The substrate can be porous or solid, planar or non-planar, unitary or distributed. The bound nucleic acid molecules may be used as hybridization probes, and may be labeled or unlabeled. In a preferred embodiment, the bound nucleic acid molecules are unlabeled.

In one embodiment, the nucleic acid molecule of the present invention is bound to a porous substrate, *e.g.*, a membrane, typically comprising nitrocellulose, nylon, or positively charged derivatized nylon. The nucleic acid molecule of the present invention can be used to detect a hybridizing nucleic acid molecule that is present within a labeled
5 nucleic acid sample, *e.g.*, a sample of transcript-derived nucleic acids. In another embodiment, the nucleic acid molecule is bound to a solid substrate, including, without limitation, glass, amorphous silicon, crystalline silicon or plastics. Examples of plastics include, without limitation, polymethylacrylic, polyethylene, polypropylene, polyacrylate, polymethylmethacrylate, polyvinylchloride, polytetrafluoroethylene, polystyrene,
10 polycarbonate, polyacetal, polysulfone, celluloseacetate, cellulosenitrate, nitrocellulose, or mixtures thereof. The solid substrate may be any shape, including rectangular, disk-like and spherical. In a preferred embodiment, the solid substrate is a microscope slide or slide-shaped substrate.

The nucleic acid molecule of the present invention can be attached covalently to a
15 surface of the support substrate or applied to a derivatized surface in a chaotropic agent that facilitates denaturation and adherence by presumed noncovalent interactions, or some combination thereof. The nucleic acid molecule of the present invention can be bound to a substrate to which a plurality of other nucleic acids are concurrently bound, hybridization to each of the plurality of bound nucleic acids being separately detectable. At low density,
20 *e.g.* on a porous membrane, these substrate-bound collections are typically denominated macroarrays; at higher density, typically on a solid support, such as glass, these substrate bound collections of plural nucleic acids are colloquially termed microarrays. As used herein, the term microarray includes arrays of all densities. It is, therefore, another aspect of the invention to provide microarrays that comprise one or more of the nucleic acid
25 molecules of the present invention.

In yet another embodiment, the invention is directed to single exon probes based on the HSNAs disclosed herein.

Expression Vectors, Host Cells and Recombinant Methods of Producing 30 Polypeptides

Another aspect of the present invention provides vectors that comprise one or more of the isolated nucleic acid molecules of the present invention, and host cells in which such vectors have been introduced.

The vectors can be used, *inter alia*, for propagating the nucleic acid molecules of the present invention in host cells (cloning vectors), for shuttling the nucleic acid molecules of the present invention between host cells derived from disparate organisms (shuttle vectors), for inserting the nucleic acid molecules of the present invention into host cell chromosomes (insertion vectors), for expressing sense or antisense RNA transcripts of the nucleic acid molecules of the present invention *in vitro* or within a host cell, and for expressing polypeptides encoded by the nucleic acid molecules of the present invention, alone or as fusion proteins with heterologous polypeptides (expression vectors). Vectors are by now well known in the art, and are described, *inter alia*, in Jones *et al.* (eds.), Vectors: Cloning Applications: Essential Techniques (Essential Techniques Series), John Wiley & Son Ltd. (1998); Jones *et al.* (eds.), Vectors: Expression Systems: Essential Techniques (Essential Techniques Series), John Wiley & Son Ltd. (1998); Gacesa *et al.*, Vectors: Essential Data, John Wiley & Sons Ltd. (1995); Cid-Arregui (eds.), Viral Vectors: Basic Science and Gene Therapy, Eaton Publishing Co. (2000); Sambrook (2001), *supra*; Ausubel (1999), *supra*. Furthermore, a variety of vectors are available commercially. Use of existing vectors and modifications thereof are well within the skill in the art. Thus, only basic features need be described here.

Nucleic acid sequences may be expressed by operatively linking them to an expression control sequence in an appropriate expression vector and employing that expression vector to transform an appropriate unicellular host. Expression control sequences are sequences that control the transcription, post-transcriptional events and translation of nucleic acid sequences. Such operative linking of a nucleic sequence of this invention to an expression control sequence, of course, includes, if not already part of the nucleic acid sequence, the provision of a translation initiation codon, ATG or GTG, in the correct reading frame upstream of the nucleic acid sequence.

A wide variety of host/expression vector combinations may be employed in expressing the nucleic acid sequences of this invention. Useful expression vectors, for example, may consist of segments of chromosomal, non-chromosomal and synthetic nucleic acid sequences.

In one embodiment, prokaryotic cells may be used with an appropriate vector. Prokaryotic host cells are often used for cloning and expression. In a preferred embodiment, prokaryotic host cells include *E. coli*, *Pseudomonas*, *Bacillus* and *Streptomyces*. In a preferred embodiment, bacterial host cells are used to express the

nucleic acid molecules of the instant invention. Useful expression vectors for bacterial hosts include bacterial plasmids, such as those from *E. coli*, *Bacillus* or *Streptomyces*, including pBluescript, pGEX-2T, pUC vectors, col E1, pCR1, pBR322, pMB9 and their derivatives, wider host range plasmids, such as RP4, phage DNAs, *e.g.*, the numerous
5 derivatives of phage lambda, *e.g.*, NM989, λ GT10 and λ GT11, and other phages, *e.g.*, M13 and filamentous single stranded phage DNA. Where *E. coli* is used as host, selectable markers are, analogously, chosen for selectivity in gram negative bacteria: *e.g.*, typical markers confer resistance to antibiotics, such as ampicillin, tetracycline, chloramphenicol, kanamycin, streptomycin and zeocin; auxotrophic markers can also be
10 used.

In other embodiments, eukaryotic host cells, such as yeast, insect, mammalian or plant cells, may be used. Yeast cells, typically *S. cerevisiae*, are useful for eukaryotic genetic studies, due to the ease of targeting genetic changes by homologous recombination and the ability to easily complement genetic defects using recombinantly expressed
15 proteins. Yeast cells are useful for identifying interacting protein components, *e.g.* through use of a two-hybrid system. In a preferred embodiment, yeast cells are useful for protein expression. Vectors of the present invention for use in yeast will typically, but not invariably, contain an origin of replication suitable for use in yeast and a selectable marker that is functional in yeast. Yeast vectors include Yeast Integrating plasmids (*e.g.*, YIp5)
20 and Yeast Replicating plasmids (the YRp and YEplac series plasmids), Yeast Centromere plasmids (the YCp series plasmids), Yeast Artificial Chromosomes (YACs) which are based on yeast linear plasmids, denoted YLp, pGPD-2, 2 μ plasmids and derivatives thereof, and improved shuttle vectors such as those described in Gietz *et al.*, *Gene*, 74: 527-34 (1988) (YIplac, YEplac and YCplac). Selectable markers in yeast vectors include
25 a variety of auxotrophic markers, the most common of which are (in *Saccharomyces cerevisiae*) URA3, HIS3, LEU2, TRP1 and LYS2, which complement specific auxotrophic mutations, such as *ura3-52*, *his3-D1*, *leu2-D1*, *trp1-D1* and *lys2-201*.

Insect cells may be chosen for high efficiency protein expression. Where the host cells are from *Spodoptera frugiperda*, *e.g.*, Sf9 and Sf21 cell lines, and expresSF™ cells
30 (Protein Sciences Corp., Meriden, CT, USA), the vector replicative strategy is typically based upon the baculovirus life cycle. Typically, baculovirus transfer vectors are used to replace the wild-type AcMNPV polyhedrin gene with a heterologous gene of interest. Sequences that flank the polyhedrin gene in the wild-type genome are positioned 5' and 3'

of the expression cassette on the transfer vectors. Following co-transfection with AcMNPV DNA, a homologous recombination event occurs between these sequences resulting in a recombinant virus carrying the gene of interest and the polyhedrin or p10 promoter. Selection can be based upon visual screening for lacZ fusion activity.

5 The host cells may also be mammalian cells, which are particularly useful for expression of proteins intended as pharmaceutical agents, and for screening of potential agonists and antagonists of a protein or a physiological pathway. Mammalian vectors intended for autonomous extrachromosomal replication will typically include a viral origin, such as the SV40 origin (for replication in cell lines expressing the large T-antigen, 10 such as COS1 and COS7 cells), the papillomavirus origin, or the EBV origin for long term episomal replication (for use, *e.g.*, in 293-EBNA cells, which constitutively express the EBV EBNA-1 gene product and adenovirus E1A). Vectors intended for integration, and thus replication as part of the mammalian chromosome, can, but need not, include an origin of replication functional in mammalian cells, such as the SV40 origin. Vectors 15 based upon viruses, such as adenovirus, adeno-associated virus, vaccinia virus, and various mammalian retroviruses, will typically replicate according to the viral replicative strategy. Selectable markers for use in mammalian cells include, include but are not limited to, resistance to neomycin (G418), blasticidin, hygromycin and zeocin, and selection based upon the purine salvage pathway using HAT medium.

20 Expression in mammalian cells can be achieved using a variety of plasmids, including pSV2, pBC12BI, and p91023, as well as lytic virus vectors (*e.g.*, vaccinia virus, adeno virus, and baculovirus), episomal virus vectors (*e.g.*, bovine papillomavirus), and retroviral vectors (*e.g.*, murine retroviruses). Useful vectors for insect cells include baculoviral vectors and pVL 941.

25 Plant cells can also be used for expression, with the vector replicon typically derived from a plant virus (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) and selectable markers chosen for suitability in plants.

 It is known that codon usage of different host cells may be different. For example, a plant cell and a human cell may exhibit a difference in codon preference for encoding a 30 particular amino acid. As a result, human mRNA may not be efficiently translated in a plant, bacteria or insect host cell. Therefore, another embodiment of this invention is directed to codon optimization. The codons of the nucleic acid molecules of the invention

may be modified to resemble, as much as possible, genes naturally contained within the host cell without altering the amino acid sequence encoded by the nucleic acid molecule.

Any of a wide variety of expression control sequences may be used in these vectors to express the nucleic acid molecules of this invention. Such useful expression control sequences include the expression control sequences associated with structural genes of the foregoing expression vectors. Expression control sequences that control transcription include, *e.g.*, promoters, enhancers and transcription termination sites. Expression control sequences in eukaryotic cells that control post-transcriptional events include splice donor and acceptor sites and sequences that modify the half-life of the transcribed RNA, *e.g.*, sequences that direct poly(A) addition or binding sites for RNA-binding proteins. Expression control sequences that control translation include ribosome binding sites, sequences which direct targeted expression of the polypeptide to or within particular cellular compartments, and sequences in the 5' and 3' untranslated regions that modify the rate or efficiency of translation.

Examples of useful expression control sequences for a prokaryote, *e.g.*, *E. coli*, will include a promoter, often a phage promoter, such as phage lambda pL promoter, the *trc* promoter, a hybrid derived from the *trp* and *lac* promoters, the bacteriophage T7 promoter (in *E. coli* cells engineered to express the T7 polymerase), the TAC or TRC system, the major operator and promoter regions of phage lambda, the control regions of *fd* coat protein, and the *araBAD* operon. Prokaryotic expression vectors may further include transcription terminators, such as the *aspA* terminator, and elements that facilitate translation, such as a consensus ribosome binding site and translation termination codon, Schomer *et al.*, *Proc. Natl. Acad. Sci. USA* 83: 8506-8510 (1986).

Expression control sequences for yeast cells, typically *S. cerevisiae*, will include a yeast promoter, such as the *CYC1* promoter, the *GAL1* promoter, the *GAL10* promoter, *ADH1* promoter, the promoters of the yeast α -mating system, or the *GPD* promoter, and will typically have elements that facilitate transcription termination, such as the transcription termination signals from the *CYC1* or *ADH1* gene.

Expression vectors useful for expressing proteins in mammalian cells will include a promoter active in mammalian cells. These promoters include, but are not limited to, those derived from mammalian viruses, such as the enhancer-promoter sequences from the immediate early gene of the human cytomegalovirus (CMV), the enhancer-promoter sequences from the Rous sarcoma virus long terminal repeat (RSV LTR), the enhancer-

promoter from SV40 and the early and late promoters of adenovirus. Other expression control sequences include the promoter for 3-phosphoglycerate kinase or other glycolytic enzymes, the promoters of acid phosphatase. Other expression control sequences include those from the gene comprising the HSNA of interest. Often, expression is enhanced by
5 incorporation of polyadenylation sites, such as the late SV40 polyadenylation site and the polyadenylation signal and transcription termination sequences from the bovine growth hormone (BGH) gene, and ribosome binding sites. Furthermore, vectors can include introns, such as intron II of rabbit β -globin gene and the SV40 splice elements.

Preferred nucleic acid vectors also include a selectable or amplifiable marker gene
10 and means for amplifying the copy number of the gene of interest. Such marker genes are well known in the art. Nucleic acid vectors may also comprise stabilizing sequences (*e.g.*, *ori*- or *ARS*-like sequences and telomere-like sequences), or may alternatively be designed to favor directed or non-directed integration into the host cell genome. In a preferred embodiment, nucleic acid sequences of this invention are inserted in frame into an
15 expression vector that allows a high level expression of an RNA which encodes a protein comprising the encoded nucleic acid sequence of interest. Nucleic acid cloning and sequencing methods are well known to those of skill in the art and are described in an assortment of laboratory manuals, including Sambrook (1989), *supra*, Sambrook (2000), *supra*; and Ausubel (1992), *supra*, Ausubel (1999), *supra*. Product information from
20 manufacturers of biological, chemical and immunological reagents also provide useful information.

Expression vectors may be either constitutive or inducible. Inducible vectors include either naturally inducible promoters, such as the *trc* promoter, which is regulated by the *lac* operon, and the *pL* promoter, which is regulated by tryptophan, the
25 MMTV-LTR promoter, which is inducible by dexamethasone, or can contain synthetic promoters and/or additional elements that confer inducible control on adjacent promoters. Examples of inducible synthetic promoters are the hybrid *Plac/ara-1* promoter and the *PLtetO-1* promoter. The *PLtetO-1* promoter takes advantage of the high expression levels from the *PL* promoter of phage lambda, but replaces the lambda repressor sites with two
30 copies of operator 2 of the *Tn10* tetracycline resistance operon, causing this promoter to be tightly repressed by the Tet repressor protein and induced in response to tetracycline (Tc) and Tc derivatives such as anhydrotetracycline. Vectors may also be inducible because they contain hormone response elements, such as the glucocorticoid response

element (GRE) and the estrogen response element (ERE), which can confer hormone inducibility where vectors are used for expression in cells having the respective hormone receptors. To reduce background levels of expression, elements responsive to ecdysone, an insect hormone, can be used instead, with coexpression of the ecdysone receptor.

5 In one embodiment of the invention, expression vectors can be designed to fuse the expressed polypeptide to small protein tags that facilitate purification and/or visualization. Such tags include a polyhistidine tag that facilitates purification of the fusion protein by immobilized metal affinity chromatography, for example using NiNTA resin (Qiagen Inc., Valencia, CA, USA) or TALON™ resin (cobalt immobilized affinity chromatography
10 medium, Clontech Labs, Palo Alto, CA, USA). The fusion protein can include a chitin-binding tag and self-excising intein, permitting chitin-based purification with self-removal of the fused tag (IMPACT™ system, New England Biolabs, Inc., Beverly, MA, USA). Alternatively, the fusion protein can include a calmodulin-binding peptide tag, permitting purification by calmodulin affinity resin (Stratagene, La Jolla, CA, USA), or a specifically
15 excisable fragment of the biotin carboxylase carrier protein, permitting purification of *in vivo* biotinylated protein using an avidin resin and subsequent tag removal (Promega, Madison, WI, USA). As another useful alternative, the polypeptides of the present invention can be expressed as a fusion to glutathione-S-transferase, the affinity and specificity of binding to glutathione permitting purification using glutathione affinity
20 resins, such as Glutathione-Superflow Resin (Clontech Laboratories, Palo Alto, CA, USA), with subsequent elution with free glutathione. Other tags include, for example, the Xpress epitope, detectable by anti-Xpress antibody (Invitrogen, Carlsbad, CA, USA), a myc tag, detectable by anti-myc tag antibody, the V5 epitope, detectable by anti-V5 antibody (Invitrogen, Carlsbad, CA, USA), FLAG® epitope, detectable by anti-FLAG®
25 antibody (Stratagene, La Jolla, CA, USA), and the HA epitope, detectable by anti-HA antibody.

For secretion of expressed polypeptides, vectors can include appropriate sequences that encode secretion signals, such as leader peptides. For example, the pSecTag2 vectors (Invitrogen, Carlsbad, CA, USA) are 5.2 kb mammalian expression vectors that carry the
30 secretion signal from the V-J2-C region of the mouse Ig kappa-chain for efficient secretion of recombinant proteins from a variety of mammalian cell lines.

Expression vectors can also be designed to fuse proteins encoded by the heterologous nucleic acid insert to polypeptides that are larger than purification and/or

identification tags. Useful protein fusions include those that permit display of the encoded protein on the surface of a phage or cell, fusions to intrinsically fluorescent proteins, such as those that have a green fluorescent protein (GFP)-like chromophore, fusions to the IgG Fc region, and fusions for use in two hybrid systems.

- 5 Vectors for phage display fuse the encoded polypeptide to, *e.g.*, the gene III protein (pIII) or gene VIII protein (pVIII) for display on the surface of filamentous phage, such as M13. *See* Barbas *et al.*, Phage Display: A Laboratory Manual, Cold Spring Harbor Laboratory Press (2001); Kay *et al.* (eds.), Phage Display of Peptides and Proteins: A Laboratory Manual, Academic Press, Inc., (1996); Abelson *et al.* (eds.), Combinatorial
 10 Chemistry (Methods in Enzymology, Vol. 267) Academic Press (1996). Vectors for yeast display, *e.g.* the pYD1 yeast display vector (Invitrogen, Carlsbad, CA, USA), use the α -agglutinin yeast adhesion receptor to display recombinant protein on the surface of *S. cerevisiae*. Vectors for mammalian display, *e.g.*, the pDisplay™ vector (Invitrogen, Carlsbad, CA, USA), target recombinant proteins using an N-terminal cell surface
 15 targeting signal and a C-terminal transmembrane anchoring domain of platelet derived growth factor receptor.

- A wide variety of vectors now exist that fuse proteins encoded by heterologous nucleic acids to the chromophore of the substrate-independent, intrinsically fluorescent green fluorescent protein from *Aequorea victoria* ("GFP") and its variants. The GFP-like
 20 chromophore can be selected from GFP-like chromophores found in naturally occurring proteins, such as *A. victoria* GFP (GenBank accession number AAA27721), *Renilla reniformis* GFP, FP583 (GenBank accession no. AF168419) (DsRed), FP593 (AF272711), FP483 (AF168420), FP484 (AF168424), FP595 (AF246709), FP486 (AF168421), FP538 (AF168423), and FP506 (AF168422), and need include only so much of the native protein
 25 as is needed to retain the chromophore's intrinsic fluorescence. Methods for determining the minimal domain required for fluorescence are known in the art. *See* Li *et al.*, *J. Biol. Chem.* 272: 28545-28549 (1997). Alternatively, the GFP-like chromophore can be selected from GFP-like chromophores modified from those found in nature. The methods for engineering such modified GFP-like chromophores and testing them for fluorescence
 30 activity, both alone and as part of protein fusions, are well known in the art. *See* Heim *et al.*, *Curr. Biol.* 6: 178-182 (1996) and Palm *et al.*, *Methods Enzymol.* 302: 378-394 (1999). A variety of such modified chromophores are now commercially available and can readily be used in the fusion proteins of the present invention. These include EGFP ("enhanced

GFP”), EBFP (“enhanced blue fluorescent protein”), BFP2, EYFP (“enhanced yellow fluorescent protein”), ECFP (“enhanced cyan fluorescent protein”) or Citrine. EGFP (*see, e.g., Cormack et al., Gene* 173: 33–38 (1996); U.S. Patent Nos. 6,090,919 and 5,804,387, the disclosures of which are incorporated herein by reference in their entireties) is found
5 on a variety of vectors, both plasmid and viral, which are available commercially (Clontech Labs, Palo Alto, CA, USA); EBFP is optimized for expression in mammalian cells whereas BFP2, which retains the original jellyfish codons, can be expressed in bacteria (*see, e.g., Heim et al., Curr. Biol.* 6: 178–182 (1996) and Cormack et al., *Gene* 173: 33–38 (1996)). Vectors containing these blue-shifted variants are available from
10 Clontech Labs (Palo Alto, CA, USA). Vectors containing EYFP, ECFP (*see, e.g., Heim et al., Curr. Biol.* 6: 178–182 (1996); Miyawaki et al., *Nature* 388: 882–887 (1997)) and Citrine (*see, e.g., Heikal et al., Proc. Natl. Acad. Sci. USA* 97: 11996–12001 (2000)) are also available from Clontech Labs. The GFP-like chromophore can also be drawn from other modified GFPs, including those described in U.S. Patent Nos. 6,124,128; 6,096,865;
15 6,090,919; 6,066,476; 6,054,321; 6,027,881; 5,968,750; 5,874,304; 5,804,387; 5,777,079; 5,741,668; and 5,625,048, the disclosures of which are incorporated herein by reference in their entireties. *See also* Conn (ed.), Green Fluorescent Protein (Methods in Enzymology, Vol. 302), Academic Press, Inc. (1999); Yang, et al., *J Biol Chem*, 273: 8212–6 (1998); Bevis et al., *Nature Biotechnology*, 20:83–7 (2002). The GFP-like chromophore of each
20 of these GFP variants can usefully be included in the fusion proteins of the present invention.

Fusions to the IgG Fc region increase serum half-life of protein pharmaceutical products through interaction with the FcRn receptor (also denominated the FcRp receptor and the Brambell receptor, FcRb), further described in International Patent Application
25 nos. WO 97/43316, WO 97/34631, WO 96/32478, WO 96/18412, the disclosures of which are incorporated herein by reference in their entireties.

For long-term, high-yield recombinant production of the polypeptides of the present invention, stable expression is preferred. Stable expression is readily achieved by integration into the host cell genome of vectors having selectable markers, followed by
30 selection of these integrants. Vectors such as pUB6/V5-His A, B, and C (Invitrogen, Carlsbad, CA, USA) are designed for high-level stable expression of heterologous proteins in a wide range of mammalian tissue types and cell lines. pUB6/V5-His uses the promoter/enhancer sequence from the human ubiquitin C gene to drive expression of

recombinant proteins: expression levels in 293, CHO, and NIH3T3 cells are comparable to levels from the CMV and human EF-1a promoters. The *bsd* gene permits rapid selection of stably transfected mammalian cells with the potent antibiotic blasticidin.

Replication incompetent retroviral vectors, typically derived from Moloney murine leukemia virus, also are useful for creating stable transfectants having integrated provirus. The highly efficient transduction machinery of retroviruses, coupled with the availability of a variety of packaging cell lines such as RetroPack™ PT 67, EcoPack2™-293, AmphoPack-293, and GP2-293 cell lines (all available from Clontech Laboratories, Palo Alto, CA, USA) allow a wide host range to be infected with high efficiency; varying the multiplicity of infection readily adjusts the copy number of the integrated provirus.

Of course, not all vectors and expression control sequences will function equally well to express the nucleic acid molecules of this invention. Neither will all hosts function equally well with the same expression system. However, one of skill in the art may make a selection among these vectors, expression control sequences and hosts without undue experimentation and without departing from the scope of this invention. For example, in selecting a vector, the host must be considered because the vector must be replicated in it. The vector's copy number, the ability to control that copy number, the ability to control integration, if any, and the expression of any other proteins encoded by the vector, such as antibiotic or other selection markers, should also be considered. The present invention further includes host cells comprising the vectors of the present invention, either present episomally within the cell or integrated, in whole or in part, into the host cell chromosome. Among other considerations, some of which are described above, a host cell strain may be chosen for its ability to process the expressed polypeptide in the desired fashion. Such post-translational modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation, and it is an aspect of the present invention to provide HSPs with such post-translational modifications.

In selecting an expression control sequence, a variety of factors should also be considered. These include, for example, the relative strength of the sequence, its controllability, and its compatibility with the nucleic acid molecules of this invention, particularly with regard to potential secondary structures. Unicellular hosts should be selected by consideration of their compatibility with the chosen vector, the toxicity of the product coded for by the nucleic acid sequences of this invention, their secretion

characteristics, their ability to fold the polypeptide correctly, their fermentation or culture requirements, and the ease of purification from them of the products coded for by the nucleic acid molecules of this invention.

5 The recombinant nucleic acid molecules and more particularly, the expression vectors of this invention may be used to express the polypeptides of this invention as recombinant polypeptides in a heterologous host cell. The polypeptides of this invention may be full-length or less than full-length polypeptide fragments recombinantly expressed from the nucleic acid molecules according to this invention. Such polypeptides include analogs, derivatives and muteins that may or may not have biological activity.

10 Vectors of the present invention will also often include elements that permit *in vitro* transcription of RNA from the inserted heterologous nucleic acid. Such vectors typically include a phage promoter, such as that from T7, T3, or SP6, flanking the nucleic acid insert. Often two different such promoters flank the inserted nucleic acid, permitting separate *in vitro* production of both sense and antisense strands.

15 Transformation and other methods of introducing nucleic acids into a host cell (*e.g.*, conjugation, protoplast transformation or fusion, transfection, electroporation, liposome delivery, membrane fusion techniques, high velocity DNA-coated pellets, viral infection and protoplast fusion) can be accomplished by a variety of methods which are well known in the art (*See*, for instance, Ausubel, *supra*, and Sambrook *et al.*, *supra*).

20 Bacterial, yeast, plant or mammalian cells are transformed or transfected with an expression vector, such as a plasmid, a cosmid, or the like, wherein the expression vector comprises the nucleic acid of interest. Alternatively, the cells may be infected by a viral expression vector comprising the nucleic acid of interest. Depending upon the host cell, vector, and method of transformation used, transient or stable expression of the
25 polypeptide will be constitutive or inducible. One having ordinary skill in the art will be able to decide whether to express a polypeptide transiently or stably, and whether to express the protein constitutively or inducibly.

A wide variety of unicellular host cells are useful in expressing the DNA sequences of this invention. These hosts may include well known eukaryotic and
30 prokaryotic hosts, such as strains of, fungi, yeast, insect cells such as *Spodoptera frugiperda* (SF9), animal cells such as CHO, as well as plant cells in tissue culture. Representative examples of appropriate host cells include, but are not limited to, bacterial cells, such as *E. coli*, *Caulobacter crescentus*, *Streptomyces* species, and *Salmonella*

typhimurium; yeast cells, such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Pichia pastoris*, *Pichia methanolica*; insect cell lines, such as those from *Spodoptera frugiperda* — e.g., Sf9 and Sf21 cell lines, and expresSFTM cells (Protein Sciences Corp., Meriden, CT, USA) — *Drosophila* S2 cells, and *Trichoplusia ni* High Five® Cells

5 (Invitrogen, Carlsbad, CA, USA); and mammalian cells. Typical mammalian cells include BHK cells, BSC 1 cells, BSC 40 cells, BMT 10 cells, VERO cells, COS1 cells, COS7 cells, Chinese hamster ovary (CHO) cells, 3T3 cells, NIH 3T3 cells, 293 cells, HEPG2 cells, HeLa cells, L cells, MDCK cells, HEK293 cells, WI38 cells, murine ES cell lines (e.g., from strains 129/SV, C57/BL6, DBA-1, 129/SVJ), K562 cells, Jurkat cells, and

10 BW5147 cells. Other mammalian cell lines are well known and readily available from the American Type Culture Collection (ATCC) (Manassas, VA, USA) and the National Institute of General Medical Sciences (NIGMS) Human Genetic Cell Repository at the Coriell Cell Repositories (Camden, NJ, USA). Cells or cell lines derived from hepatic are particularly preferred because they may provide a more native post-translational

15 processing. Particularly preferred are human hepatic cells.

Particular details of the transfection, expression and purification of recombinant proteins are well documented and are understood by those of skill in the art. Further details on the various technical aspects of each of the steps used in recombinant production of foreign genes in bacterial cell expression systems can be found in a number

20 of texts and laboratory manuals in the art. See, e.g., Ausubel (1992), *supra*, Ausubel (1999), *supra*, Sambrook (1989), *supra*, and Sambrook (2001), *supra*.

Methods for introducing the vectors and nucleic acid molecules of the present invention into the host cells are well known in the art; the choice of technique will depend primarily upon the specific vector to be introduced and the host cell chosen.

25 Nucleic acid molecules and vectors may be introduced into prokaryotes, such as *E. coli*, in a number of ways. For instance, phage lambda vectors will typically be packaged using a packaging extract (e.g., Gigapack® packaging extract, Stratagene, La Jolla, CA, USA), and the packaged virus used to infect *E. coli*.

Plasmid vectors will typically be introduced into chemically competent or

30 electrocompetent bacterial cells. *E. coli* cells can be rendered chemically competent by treatment, e.g., with CaCl₂, or a solution of Mg²⁺, Mn²⁺, Ca²⁺, Rb⁺ or K⁺, dimethyl sulfoxide, dithiothreitol, and hexamine cobalt (III), Hanahan, *J. Mol. Biol.* 166(4):557-80 (1983), and vectors introduced by heat shock. A wide variety of chemically competent

strains are also available commercially (e.g., Epicurian Coli® XL10-Gold® Ultracompetent Cells (Stratagene, La Jolla, CA, USA); DH5α competent cells (Clontech Laboratories, Palo Alto, CA, USA); and TOP10 Chemically Competent E. coli Kit (Invitrogen, Carlsbad, CA, USA)). Bacterial cells can be rendered electrocompetent to
5 take up exogenous DNA by electroporation by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided by BioRad (Richmond, CA, USA).

Vectors can be introduced into yeast cells by spheroplasting, treatment with lithium salts, electroporation, or protoplast fusion. Spheroplasts are prepared by the action
10 of hydrolytic enzymes such as a snail-gut extract, usually denoted Glusulase or Zymolyase, or an enzyme from *Arthrobacter luteus* to remove portions of the cell wall in the presence of osmotic stabilizers, typically 1 M sorbitol. DNA is added to the spheroplasts, and the mixture is co-precipitated with a solution of polyethylene glycol (PEG) and Ca^{2+} . Subsequently, the cells are resuspended in a solution of sorbitol, mixed
15 with molten agar and then layered on the surface of a selective plate containing sorbitol.

For lithium-mediated transformation, yeast cells are treated with lithium acetate to permeabilize the cell wall, DNA is added and the cells are co-precipitated with PEG. The cells are exposed to a brief heat shock, washed free of PEG and lithium acetate, and subsequently spread on plates containing ordinary selective medium. Increased
20 frequencies of transformation are obtained by using specially-prepared single-stranded carrier DNA and certain organic solvents. Schiestl *et al.*, *Curr. Genet.* 16(5-6): 339-46 (1989).

For electroporation, freshly-grown yeast cultures are typically washed, suspended in an osmotic protectant, such as sorbitol, mixed with DNA, and the cell suspension
25 pulsed in an electroporation device. Subsequently, the cells are spread on the surface of plates containing selective media. Becker *et al.*, *Methods Enzymol.* 194: 182-187 (1991). The efficiency of transformation by electroporation can be increased over 100-fold by using PEG, single-stranded carrier DNA and cells that are in late log-phase of growth. Larger constructs, such as YACs, can be introduced by protoplast fusion.

30 Mammalian and insect cells can be directly infected by packaged viral vectors, or transfected by chemical or electrical means. For chemical transfection, DNA can be coprecipitated with CaPO_4 or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for CaPO_4 transfection (CalPhos™ Mammalian

Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER, (Roche Molecular Biochemicals, Indianapolis, IN USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA). Protocols for electroporating mammalian cells can be found in, for example, ; Norton *et al.* (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000). Other transfection techniques include transfection by particle bombardment and microinjection. See, e.g., Cheng *et al.*, *Proc. Natl. Acad. Sci. USA* 90(10): 4455-9 (1993); Yang *et al.*, *Proc. Natl. Acad. Sci. USA* 87(24): 9568-72 (1990).

Production of the recombinantly produced proteins of the present invention can optionally be followed by purification.

Purification of recombinantly expressed proteins is now well within the skill in the art and thus need not be detailed here. See, e.g., Thorner *et al.* (eds.), Applications of Chimeric Genes and Hybrid Proteins, Part A: Gene Expression and Protein Purification (Methods in Enzymology, Vol. 326), Academic Press (2000); Harbin (ed.), Cloning, Gene Expression and Protein Purification : Experimental Procedures and Process Rationale, Oxford Univ. Press (2001); Marshak *et al.*, Strategies for Protein Purification and Characterization: A Laboratory Course Manual, Cold Spring Harbor Laboratory Press (1996); and Roe (ed.), Protein Purification Applications, Oxford University Press (2001).

Briefly, however, if purification tags have been fused through use of an expression vector that appends such tag, purification can be effected, at least in part, by means appropriate to the tag, such as use of immobilized metal affinity chromatography for polyhistidine tags. Other techniques common in the art include ammonium sulfate fractionation, immunoprecipitation, fast protein liquid chromatography (FPLC), high performance liquid chromatography (HPLC), and preparative gel electrophoresis.

Polypeptides, including Fragments Muteins, Homologous Proteins, Allelic Variants, Analogs and Derivatives

Another aspect of the invention relates to polypeptides encoded by the nucleic acid molecules described herein. In a preferred embodiment, the polypeptide is a hepatic

specific polypeptide (HSP). In an even more preferred embodiment, the polypeptide comprises an amino acid sequence of SEQ ID NO:410-611 or is derived from a polypeptide having the amino acid sequence of SEQ ID NO: 410-611. A polypeptide as defined herein may be produced recombinantly, as discussed *supra*, may be isolated from a cell that naturally expresses the protein, or may be chemically synthesized following the teachings of the specification and using methods well known to those having ordinary skill in the art.

Polypeptides of the present invention may also comprise a part or fragment of a HSP. In a preferred embodiment, the fragment is derived from a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 410-611. Polypeptides of the present invention comprising a part or fragment of an entire HSP may or may not be HSPs. For example, a full-length polypeptide may be hepatic-specific, while a fragment thereof may be found in other tissues as well as in hepatic. A polypeptide that is not a HSP, whether it is a fragment, analog, mutein, homologous protein or derivative, is nevertheless useful, especially for immunizing animals to prepare anti-HSP antibodies. In a preferred embodiment, the part or fragment is a HSP. Methods of determining whether a polypeptide of the present invention is a HSP are described *infra*.

Polypeptides of the present invention comprising fragments of at least 6 contiguous amino acids are also useful in mapping B cell and T cell epitopes of the reference protein. See, e.g., Geysen *et al.*, *Proc. Natl. Acad. Sci. USA* 81: 3998-4002 (1984) and U.S. Patent Nos. 4,708,871 and 5,595,915, the disclosures of which are incorporated herein by reference in their entireties. Because the fragment need not itself be immunogenic, part of an immunodominant epitope, nor even recognized by native antibody, to be useful in such epitope mapping, all fragments of at least 6 amino acids of a polypeptide of the present invention have utility in such a study.

Polypeptides of the present invention comprising fragments of at least 8 contiguous amino acids, often at least 15 contiguous amino acids, are useful as immunogens for raising antibodies that recognize polypeptides of the present invention. See, e.g., Lerner, *Nature* 299: 592-596 (1982); Shinnick *et al.*, *Annu. Rev. Microbiol.* 37: 425-46 (1983); Sutcliffe *et al.*, *Science* 219: 660-6 (1983). As further described in the above-cited references, virtually all 8-mers, conjugated to a carrier, such as a protein, prove immunogenic and are capable of eliciting antibody for the conjugated peptide;

accordingly, all fragments of at least 8 amino acids of the polypeptides of the present invention have utility as immunogens.

Polypeptides comprising fragments of at least 8, 9, 10 or 12 contiguous amino acids are also useful as competitive inhibitors of binding of the entire polypeptide, or a portion thereof, to antibodies (as in epitope mapping), and to natural binding partners, such as subunits in a multimeric complex or to receptors or ligands of the subject protein; this competitive inhibition permits identification and separation of molecules that bind specifically to the polypeptide of interest. See U.S. Patent Nos. 5,539,084 and 5,783,674, incorporated herein by reference in their entireties.

The polypeptide of the present invention thus preferably is at least 6 amino acids in length, typically at least 8, 9, 10 or 12 amino acids in length, and often at least 15 amino acids in length. Often, the polypeptide of the present invention is at least 20 amino acids in length, even 25 amino acids, 30 amino acids, 35 amino acids, or 50 amino acids or more in length. Of course, larger polypeptides having at least 75 amino acids, 100 amino acids, or even 150 amino acids are also useful, and at times preferred.

One having ordinary skill in the art can produce fragments by truncating the nucleic acid molecule, *e.g.*, a HSNA, encoding the polypeptide and then expressing it recombinantly. Alternatively, one can produce a fragment by chemically synthesizing a portion of the full-length polypeptide. One may also produce a fragment by enzymatically cleaving either a recombinant polypeptide or an isolated naturally occurring polypeptide. Methods of producing polypeptide fragments are well known in the art. *See, e.g.*, Sambrook (1989), *supra*; Sambrook (2001), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), *supra*. In one embodiment, a polypeptide comprising only a fragment, preferably a fragment of a HSP, may be produced by chemical or enzymatic cleavage of a HSP polypeptide. In a preferred embodiment, a polypeptide fragment is produced by expressing a nucleic acid molecule of the present invention encoding a fragment, preferably of a HSP, in a host cell.

Polypeptides of the present invention are also inclusive of mutants, fusion proteins, homologous proteins and allelic variants.

A mutant protein, or mutein, may have the same or different properties compared to a naturally occurring polypeptide and comprises at least one amino acid insertion, duplication, deletion, rearrangement or substitution compared to the amino acid sequence of a native polypeptide. Small deletions and insertions can often be found that do not alter

the function of a protein. Muteins may or may not be hepatic-specific. Preferably, the mutein is hepatic-specific. More preferably the mutein is a polypeptide that comprises at least one amino acid insertion, duplication, deletion, rearrangement or substitution compared to the amino acid sequence of SEQ ID NO: 410-611. Accordingly, in a preferred embodiment, the mutein is one that exhibits at least 50% sequence identity, more preferably at least 60% sequence identity, even more preferably at least 70%, yet more preferably at least 80% sequence identity to a HSP comprising an amino acid sequence of SEQ ID NO: 410-611. In a yet more preferred embodiment, the mutein exhibits at least 85%, more preferably 90%, even more preferably 95% or 96%, and yet more preferably at least 97%, 98%, 99% or 99.5% sequence identity to a HSP comprising an amino acid sequence of SEQ ID NO: 410-611.

A mutein may be produced by isolation from a naturally occurring mutant cell, tissue or organism. A mutein may be produced by isolation from a cell, tissue or organism that has been experimentally mutagenized. Alternatively, a mutein may be produced by chemical manipulation of a polypeptide, such as by altering the amino acid residue to another amino acid residue using synthetic or semi-synthetic chemical techniques. In a preferred embodiment, a mutein is produced from a host cell comprising a mutated nucleic acid molecule compared to the naturally occurring nucleic acid molecule. For instance, one may produce a mutein of a polypeptide by introducing one or more mutations into a nucleic acid molecule of the invention and then expressing it recombinantly. These mutations may be targeted, in which particular encoded amino acids are altered, or may be untargeted, in which random encoded amino acids within the polypeptide are altered. Muteins with random amino acid alterations can be screened for a particular biological activity or property, particularly whether the polypeptide is hepatic-specific, as described below. Multiple random mutations can be introduced into the gene by methods well known to the art, *e.g.*, by error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis and site-specific mutagenesis. Methods of producing muteins with targeted or random amino acid alterations are well known in the art. *See, e.g.*, Sambrook (1989), *supra*; Sambrook (2001), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), as well as U.S. Patent No. 5,223,408, which is herein incorporated by reference in its entirety.

The invention also contemplates polypeptides that are homologous to a polypeptide of the invention. In a preferred embodiment, the polypeptide is homologous to a HSP. In an even more preferred embodiment, the polypeptide is homologous to a HSP selected from the group having an amino acid sequence of SEQ ID NO: 410-611. By
5 homologous polypeptide it is means one that exhibits significant sequence identity to a HSP, preferably a HSP having an amino acid sequence of SEQ ID NO: 410-611. By significant sequence identity it is meant that the homologous polypeptide exhibits at least 50% sequence identity, more preferably at least 60% sequence identity, even more preferably at least 70%, yet more preferably at least 80% sequence identity to a HSP
10 comprising an amino acid sequence of SEQ ID NO: 410-611. More preferred are homologous polypeptides exhibiting at least 85%, more preferably 90%, even more preferably 95% or 96%, and yet more preferably at least 97% or 98% sequence identity to a HSP comprising an amino acid sequence of SEQ ID NO: 410-611. Most preferably, the homologous polypeptide exhibits at least 99%, more preferably 99.5%, even more
15 preferably 99.6%, 99.7%, 99.8% or 99.9% sequence identity to a HSP comprising an amino acid sequence of SEQ ID NO: 410-611. In a preferred embodiment, the amino acid substitutions of the homologous polypeptide are conservative amino acid substitutions as discussed above.

Homologous polypeptides of the present invention also comprise polypeptide
20 encoded by a nucleic acid molecule that selectively hybridizes to a HSNA or an antisense sequence thereof. In this embodiment, it is preferred that the homologous polypeptide be encoded by a nucleic acid molecule that hybridizes to a HSNA under low stringency, moderate stringency or high stringency conditions, as defined herein. More preferred is a homologous polypeptide encoded by a nucleic acid sequence which hybridizes to a HSNA
25 selected from the group consisting of SEQ ID NO: 1-409 or a homologous polypeptide encoded by a nucleic acid molecule that hybridizes to a nucleic acid molecule that encodes a HSP, preferably an HSP of SEQ ID NO: 410-611 under low stringency, moderate stringency or high stringency conditions, as defined herein.

Homologous polypeptides of the present invention may be naturally occurring and
30 derived from another species, especially one derived from another primate, such as chimpanzee, gorilla, rhesus macaque, or baboon, wherein the homologous polypeptide comprises an amino acid sequence that exhibits significant sequence identity to that of SEQ ID NO: 410-611. The homologous polypeptide may also be a naturally occurring

polypeptide from a human, when the HSP is a member of a family of polypeptides. The homologous polypeptide may also be a naturally occurring polypeptide derived from a non-primate, mammalian species, including without limitation, domesticated species, *e.g.*, dog, cat, mouse, rat, rabbit, guinea pig, hamster, cow, horse, goat or pig. The homologous polypeptide may also be a naturally occurring polypeptide derived from a non-mammalian species, such as birds or reptiles. The naturally occurring homologous protein may be isolated directly from humans or other species. Alternatively, the nucleic acid molecule encoding the naturally occurring homologous polypeptide may be isolated and used to express the homologous polypeptide recombinantly. The homologous polypeptide may also be one that is experimentally produced by random mutation of a nucleic acid molecule and subsequent expression of the nucleic acid molecule. Alternatively, the homologous polypeptide may be one that is experimentally produced by directed mutation of one or more codons to alter the encoded amino acid of a HSP. In a preferred embodiment, the homologous polypeptide encodes a polypeptide that is a HSP.

Relatedness of proteins can also be characterized using a second functional test, the ability of a first protein competitively to inhibit the binding of a second protein to an antibody. It is, therefore, another aspect of the present invention to provide isolated polypeptide not only identical in sequence to those described with particularity herein, but also to provide isolated polypeptide ("cross-reactive proteins") that competitively inhibit the binding of antibodies to all or to a portion of various of the isolated polypeptides of the present invention. Such competitive inhibition can readily be determined using immunoassays well known in the art.

As discussed above, single nucleotide polymorphisms (SNPs) occur frequently in eukaryotic genomes, and the sequence determined from one individual of a species may differ from other allelic forms present within the population. Thus, polypeptides of the present invention are also inclusive of those encoded by an allelic variant of a nucleic acid molecule encoding a HSP. In this embodiment, it is preferred that the polypeptide be encoded by an allelic variant of a gene that encodes a polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO: 410-611. More preferred is that the polypeptide be encoded by an allelic variant of a gene that has the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1-409.

Polypeptides of the present invention are also inclusive of derivative polypeptides encoded by a nucleic acid molecule according to the instant invention. In this

embodiment, it is preferred that the polypeptide be a HSP. Also preferred are derivative polypeptides having an amino acid sequence selected from the group consisting of SEQ ID NO: 410-611 and which has been acetylated, carboxylated, phosphorylated, glycosylated, ubiquitinated or other PTMs. In another preferred embodiment, the derivative has been labeled with, *e.g.*, radioactive isotopes such as ^{125}I , ^{32}P , ^{35}S , and ^3H . In another preferred embodiment, the derivative has been labeled with fluorophores, chemiluminescent agents, enzymes, and antiligands that can serve as specific binding pair members for a labeled ligand.

Polypeptide modifications are well known to those of skill and have been described in great detail in the scientific literature. Several particularly common modifications, glycosylation, lipid attachment, sulfation, gamma-carboxylation of glutamic acid residues, hydroxylation and ADP-ribosylation, for instance, are described in most basic texts, such as, for instance Creighton, Protein Structure and Molecular Properties, 2nd ed., W. H. Freeman and Company (1993). Many detailed reviews are available on this subject, such as, for example, those provided by Wold, in Johnson (ed.), Posttranslational Covalent Modification of Proteins, pgs. 1-12, Academic Press (1983); Seifter *et al.*, *Meth. Enzymol.* 182: 626-646 (1990) and Rattan *et al.*, *Ann. N.Y. Acad. Sci.* 663: 48-62 (1992).

One may determine whether a polypeptide of the invention is likely to be post-translationally modified by analyzing the sequence of the polypeptide to determine if there are peptide motifs indicative of sites for post-translational modification. There are a number of computer programs that permit prediction of post-translational modifications. See, *e.g.*, www.expasy.org (accessed November 11, 2002), which includes PSORT, for prediction of protein sorting signals and localization sites, SignalP, for prediction of signal peptide cleavage sites, MITOPROT and Predotar, for prediction of mitochondrial targeting sequences, NetOGlyc, for prediction of type O-glycosylation sites in mammalian proteins, big-PI Predictor and DGPI, for prediction of prenylation-anchor and cleavage sites, and NetPhos, for prediction of Ser, Thr and Tyr phosphorylation sites in eukaryotic proteins. Other computer programs, such as those included in GCG, also may be used to determine post-translational modification peptide motifs.

General examples of types of post-translational modifications include, but are not limited to: (Z)-dehydrobutyrine; 1-chondroitin sulfate-L-aspartic acid ester; 1'-glycosyl-L-tryptophan; 1'-phospho-L-histidine; 1-thioglycine; 2'-(S-L-cysteinyl)-L-histidine; 2'-[3-

carboxamido (trimethylammonio)propyl]-L-histidine; 2'-alpha-mannosyl-L-tryptophan; 2-methyl-L-glutamine; 2-oxobutanoic acid; 2-pyrrolidone carboxylic acid; 3'-(1'-L-histidyl)-L-tyrosine; 3'-(8alpha-FAD)-L-histidine; 3'-(S-L-cysteinyl)-L-tyrosine; 3', 3'', 5'-triiodo-L-tyrosine; 3'-4'-phospho-L-tyrosine; 3-hydroxy-L-proline; 3'-methyl-L-histidine; 3-
 5 methyl-L-lanthionine; 3'-phospho-L-histidine; 4'-(L-tryptophan)-L-tryptophyl quinone; 42 N-cysteinyl-glycosylphosphatidylinositoethanolamine; 43 -(T-L-histidyl)-L-tyrosine; 4-hydroxy-L-arginine; 4-hydroxy-L-lysine; 4-hydroxy-L-proline; 5'-(N6-L-lysine)-L-topaquinone; 5-hydroxy-L-lysine; 5-methyl-L-arginine; alpha-I-microglobulin-Ig alpha complex chromophore; bis-L-cysteinyl bis-L-histidino diiron disulfide; bis-L--cysteinyl-L-
 10 N3'-histidino-L-serinyl tetrairon' tetrasulfide; chondroitin sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; D-alanine; D-allo-isoleucine; D-asparagine; dehydroalanine; dehydrotyrosine; dermatan 4-sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; D-glucuronyl-N-glycine; dipyrrolylmethanemethyl-L-cysteine; D-leucine; D-methionine; D-phenylalanine; D-serine; D-tryptophan; glycine
 15 amide; glycine oxazolecarboxylic acid; glycine thiazolecarboxylic acid; heme P450-bis-L-cysteine-L-tyrosine; heme-bis-L-cysteine; hemediol-L-aspartyl ester-L-glutamyl ester; hemediol-L-aspartyl ester-L-glutamyl ester-L-methionine sulfonium; heme-L-cysteine; heme-L-histidine; heparan sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; heme P450-bis-L-cysteine-L-lysine; hexakis-L-cysteinyl hexairon hexasulfide;
 20 keratan sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-threonine; L-oxoalanine- lactic acid; L phenyllactic acid; l'-(8alpha-FAD)-L-histidine; L-2'.4'.5'-topaquinone; L-3',4'-dihydroxyphenylalanine; L-3'.4'.5'-trihydroxyphenylalanine; L-4'-bromophenylalanine; L-6'-bromotryptophan; L-alanine amide; L-alanyl imidazolinone glycine; L-allysine; L-arginine amide; L-asparagine amide; L-aspartic 4-phosphoric
 25 anhydride; L-aspartic acid 1-amide; L-beta-methylthioaspartic acid; L-bromohistidine; L-citrulline; L-cysteine amide; L-cysteine glutathione disulfide; L-cysteine methyl disulfide; L-cysteine methyl ester; L-cysteine oxazolecarboxylic acid; L-cysteine oxazolinecarboxylic acid; L-cysteine persulfide; L-cysteine sulfenic acid; L-cysteine sulfinic acid; L-cysteine thiazolecarboxylic acid; L-cysteinyl homocitryl molybdenum-
 30 heptairon-nonasulfide; L-cysteinyl imidazolinone glycine; L-cysteinyl molybdopterin; L-cysteinyl molybdopterin guanine dinucleotide; L-cystine; L-erythro-beta-hydroxyasparagine; L-erythro-beta-hydroxyaspartic acid; L-gamma-carboxyglutamic acid; L-glutamic acid 1-amide; L-glutamic acid 5-methyl ester; L-glutamine amide; L-glutamyl

5-glycerylphosphorylethanolamine; L-histidine amide; L-isoglutamyl-polyglutamic acid; L-isoglutamyl-polyglycine; L-isoleucine amide; L-lanthionine; L-leucine amide; L-lysine amide; L-lysine thiazolecarboxylic acid; L-lysinoalanine; L-methionine amide; L-methionine sulfone; L-phenylalanine thiazolecarboxylic acid; L-phenylalanine amide; L-proline amide; L-selenocysteine; L-selenocysteinyl molybdopterin guanine dinucleotide; L-serine amide; L-serine thiazolecarboxylic acid; L-seryl imidazolinone glycine; L-T-bromophenylalanine; L-T-bromophenylalanine; L-threonine amide; L-thyroxine; L-tryptophan amide; L-tryptophyl quinone; L-tyrosine amide; L-valine amide; meso-lanthionine; N-(L-glutamyl)-L-tyrosine; N-(L-isoaspartyl)-glycine; N-(L-isoaspartyl)-L-cysteine; N,N,N-trimethyl-L-alanine; N,N-dimethyl-L-proline; N2-acetyl-L-lysine; N2-succinyl-L-tryptophan; N4-(ADP-ribosyl)-L-asparagine; N4-glycosyl-L-asparagine; N4-hydroxymethyl-L-asparagine; N4-methyl-L-asparagine; N5-methyl-L-glutamine; N6-1-carboxyethyl-L-lysine; N6-(4-amino hydroxybutyl)-L-lysine; N6-(L-isoglutamyl)-L-lysine; N6-(phospho-5'-adenosine)-L-lysine; N6-(phospho-5'-guanosine)-L-lysine; N6,N6,N6-trimethyl-L-lysine; N6,N6-dimethyl-L-lysine; N6-acetyl-L-lysine; N6-biotinyl-L-lysine; N6-carboxy-L-lysine; N6-formyl-L-lysine; N6-glycyl-L-lysine; N6-lipoyl-L-lysine; N6-methyl-L-lysine; N6-methyl-N6-poly(N-methyl-propylamine)-L-lysine; N6-mureinyl-L-lysine; N6-myristoyl-L-lysine; N6-palmitoyl-L-lysine; N6-pyridoxal phosphate-L-lysine; N6-pyruvic acid 2-iminyl-L-lysine; N6-retinal-L-lysine; N-acetyl-glycine; N-acetyl-L-glutamine; N-acetyl-L-alanine; N-acetyl-L-aspartic acid; N-acetyl-L-cysteine; N-acetyl-L-glutamic acid; N-acetyl-L-isoleucine; N-acetyl-L-methionine; N-acetyl-L-proline; N-acetyl-L-serine; N-acetyl-L-threonine; N-acetyl-L-tyrosine; N-acetyl-L-valine; N-alanyl-glycosylphosphatidylinositoethanolamine; N-asparaginyl-glycosylphosphatidylinositoethanolamine; N-aspartyl-glycosylphosphatidylinositoethanolamine; N-formylglycine; N-formyl-L-methionine; N-glycyl-glycosylphosphatidylinositoethanolamine; N-L-glutamyl-poly-L-glutamic acid; N-methylglycine; N-methyl-L-alanine; N-methyl-L-methionine; N-methyl-L-phenylalanine; N-myristoyl-glycine; N-palmitoyl-L-cysteine; N-pyruvic acid 2-iminyl-L-cysteine; N-pyruvic acid 2-iminyl-L-valine; N-seryl-glycosylphosphatidylinositoethanolamine; N-seryl-glycosylHSPHINGOLIPIDINOSITOETHANOLAMINE; O-(ADP-ribosyl)-L-serine; O-(phospho-5'-adenosine)-L-threonine; O-(phospho-5'-DNA)-L-serine; O-(phospho-5'-DNA)-L-threonine; O-(phospho-5'tRNA)-L-serine; O-(phosphoribosyl dephospho-coenzyme A)-L-serine; O-(sn-1-glycerophosphoryl)-L-serine; O4'-(8alpha-FAD)-L-tyrosine; O4'-(phospho-

5'-adenosine)-L-tyrosine; O4'-(phospho-5'-DNA)-L-tyrosine; O4'-(phospho-5'-RNA)-L-tyrosine; O4'-(phospho-5'-uridine)-L-tyrosine; O4-glycosyl-L-hydroxyproline; O4'-glycosyl-L-tyrosine; O4'-sulfo-L-tyrosine; O5-glycosyl-L-hydroxylysine; O-glycosyl-L-serine; O-glycosyl-L-threonine; omega-N-(ADP-ribosyl)-L-arginine; omega-N-omega-N'-dimethyl-L-arginine; omega-N-methyl-L-arginine; omega-N-omega-N-dimethyl-L-arginine; omega-N-phospho-L-arginine; O-octanoyl-L-serine; O-palmitoyl-L-serine; O-palmitoyl-L-threonine; O-phospho-L-serine; O-phospho-L-threonine; O-phosphopantetheine-L-serine; phycoerythrobilin-bis-L-cysteine; phycourobilin-bis-L-cysteine; pyrroloquinoline quinone; pyruvic acid; S hydroxycinnamyl-L-cysteine; S-(2-aminovinyl) methyl-D-cysteine; S-(2-aminovinyl)-D-cysteine; S-(6-FW-L-cysteine; S-(8alpha-FAD)-L-cysteine; S-(ADP-ribosyl)-L-cysteine; S-(L-isoglutamyl)-L-cysteine; S-12-hydroxyfarnesyl-L-cysteine; S-acetyl-L-cysteine; S-diacylglycerol-L-cysteine; S-diphytanylglycerol diether-L-cysteine; S-farnesyl-L-cysteine; S-geranylgeranyl-L-cysteine; S-glycosyl-L-cysteine; S-glycyl-L-cysteine; S-methyl-L-cysteine; S-nitrosyl-L-cysteine; S-palmitoyl-L-cysteine; S-phospho-L-cysteine; S-phycobiliviolin-L-cysteine; S-phycocyanobilin-L-cysteine; S-phycoerythrobilin-L-cysteine; S-phytochromobilin-L-cysteine; S-selenyl-L-cysteine; S-sulfo-L-cysteine; tetrakis-L-cysteiny diiron disulfide; tetrakis-L-cysteiny iron; tetrakis-L-cysteiny tetrairon tetrasulfide; trans-2,3-cis 4-dihydroxy-L-proline; tris-L-cysteiny triiron tetrasulfide; tris-L-cysteiny triiron trisulfide; tris-L-cysteiny-L-aspartato tetrairon tetrasulfide; tris-L-cysteiny-L-cysteine persulfido-bis-L-glutamato-L-histidino tetrairon disulfide trioxide; tris-L-cysteiny-L-N3'-histidino tetrairon tetrasulfide; tris-L-cysteiny-L-N1'-histidino tetrairon tetrasulfide; and tris-L-cysteiny-L-seriny tetrairon tetrasulfide.

Additional examples of PTMs may be found in web sites such as the Delta Mass database based on Krishna, R. G. and F. Wold (1998). Posttranslational Modifications. Proteins - Analysis and Design. R. H. Angeletti. San Diego, Academic Press. 1: 121-206. ; Methods in Enzymology, 193, J.A. McClosky (ed) (1990), pages 647-660; Methods in Protein Sequence Analysis edited by Kazutomo Imahori and Fumio Sakiyama, Plenum Press, (1993) "Post-translational modifications of proteins" R.G. Krishna and F. Wold pages 167-172; "GlycoSuiteDB: a new curated relational database of glycoprotein glycan structures and their biological sources" Cooper et al. Nucleic Acids Res. 29; 332-335 (2001) "O-GLYCBASE version 4.0: a revised database of O-glycosylated proteins" Gupta et al. Nucleic Acids Research, 27: 370-372 (1999); and "PhosphoBase, a database of

phosphorylation sites: release 2.0.", Kreegipuu et al. *Nucleic Acids Res* 27(1):237-239 (1999) see also, WO 02/21139A2, the disclosure of which is incorporated herein by reference in its entirety.

Tumorigenesis is often accompanied by alterations in the post-translational
5 modifications of proteins. Thus, in another embodiment, the invention provides polypeptides from cancerous cells or tissues that have altered post-translational modifications compared to the post-translational modifications of polypeptides from normal cells or tissues. A number of altered post-translational modifications are known. One common alteration is a change in phosphorylation state, wherein the polypeptide from
10 the cancerous cell or tissue is hyperphosphorylated or hypophosphorylated compared to the polypeptide from a normal tissue, or wherein the polypeptide is phosphorylated on different residues than the polypeptide from a normal cell. Another common alteration is a change in glycosylation state, wherein the polypeptide from the cancerous cell or tissue has more or less glycosylation than the polypeptide from a normal tissue, and/or wherein
15 the polypeptide from the cancerous cell or tissue has a different type of glycosylation than the polypeptide from a noncancerous cell or tissue. Changes in glycosylation may be critical because carbohydrate-protein and carbohydrate-carbohydrate interactions are important in cancer cell progression, dissemination and invasion. See, e.g., Barchi, *Curr. Pharm. Des.* 6: 485-501 (2000), Verma, *Cancer Biochem. Biophys.* 14: 151-162 (1994)
20 and Dennis et al., *Bioessays* 5: 412-421 (1999).

Another post-translational modification that may be altered in cancer cells is prenylation. Prenylation is the covalent attachment of a hydrophobic prenyl group (either farnesyl or geranylgeranyl) to a polypeptide. Prenylation is required for localizing a protein to a cell membrane and is often required for polypeptide function. For instance,
25 the Ras superfamily of GTPase signalling proteins must be prenylated for function in a cell. See, e.g., Prendergast et al., *Semin. Cancer Biol.* 10: 443-452 (2000) and Khwaja et al., *Lancet* 355: 741-744 (2000).

Other post-translation modifications that may be altered in cancer cells include, without limitation, polypeptide methylation, acetylation, arginylation or racemization of
30 amino acid residues. In these cases, the polypeptide from the cancerous cell may exhibit either increased or decreased amounts of the post-translational modification compared to the corresponding polypeptides from noncancerous cells.

Other polypeptide alterations in cancer cells include abnormal polypeptide cleavage of proteins and aberrant protein-protein interactions. Abnormal polypeptide cleavage may be cleavage of a polypeptide in a cancerous cell that does not usually occur in a normal cell, or a lack of cleavage in a cancerous cell, wherein the polypeptide is
5 cleaved in a normal cell. Aberrant protein-protein interactions may be either covalent cross-linking or non-covalent binding between proteins that do not normally bind to each other. Alternatively, in a cancerous cell, a protein may fail to bind to another protein to which it is bound in a noncancerous cell. Alterations in cleavage or in protein-protein interactions may be due to over- or underproduction of a polypeptide in a cancerous cell
10 compared to that in a normal cell, or may be due to alterations in post-translational modifications (see above) of one or more proteins in the cancerous cell. See, e.g., Henschen-Edman, *Ann. N.Y. Acad. Sci.* 936: 580-593 (2001).

Alterations in polypeptide post-translational modifications, as well as changes in polypeptide cleavage and protein-protein interactions, may be determined by any method
15 known in the art. For instance, alterations in phosphorylation may be determined by using anti-phosphoserine, anti-phosphothreonine or anti-phosphotyrosine antibodies or by amino acid analysis. Glycosylation alterations may be determined using antibodies specific for different sugar residues, by carbohydrate sequencing, or by alterations in the size of the glycoprotein, which can be determined by, e.g., SDS polyacrylamide gel electrophoresis
20 (PAGE). Other alterations of post-translational modifications, such as prenylation, racemization, methylation, acetylation and arginylation, may be determined by chemical analysis, protein sequencing, amino acid analysis, or by using antibodies specific for the particular post-translational modifications. Changes in protein-protein interactions and in polypeptide cleavage may be analyzed by any method known in the art including, without
25 limitation, non-denaturing PAGE (for non-covalent protein-protein interactions), SDS PAGE (for covalent protein-protein interactions and protein cleavage), chemical cleavage, protein sequencing or immunoassays.

In another embodiment, the invention provides polypeptides that have been post-translationally modified. In one embodiment, polypeptides may be modified
30 enzymatically or chemically, by addition or removal of a post-translational modification. For example, a polypeptide may be glycosylated or deglycosylated enzymatically. Similarly, polypeptides may be phosphorylated using a purified kinase, such as a MAP kinase (e.g., p38, ERK, or JNK) or a tyrosine kinase (e.g., Src or erbB2). A polypeptide

may also be modified through synthetic chemistry. Alternatively, one may isolate the polypeptide of interest from a cell or tissue that expresses the polypeptide with the desired post-translational modification. In another embodiment, a nucleic acid molecule encoding the polypeptide of interest is introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide in the desired fashion. If the polypeptide does not contain a motif for a desired post-translational modification, one may alter the post-translational modification by mutating the nucleic acid sequence of a nucleic acid molecule encoding the polypeptide so that it contains a site for the desired post-translational modification. Amino acid sequences that may be post-translationally modified are known in the art. See, e.g., the programs described above on the website www.expasy.org. The nucleic acid molecule may also be introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide. Similarly, one may delete sites that are post-translationally modified by either mutating the nucleic acid sequence so that the encoded polypeptide does not contain the post-translational modification motif, or by introducing the native nucleic acid molecule into a host cell that is not capable of post-translationally modifying the encoded polypeptide.

It will be appreciated, as is well known and as noted above, that polypeptides are not always entirely linear. For instance, polypeptides may be branched as a result of ubiquitination, and they may be circular, with or without branching, generally as a result of posttranslation events, including natural processing event and events brought about by human manipulation which do not occur naturally. Circular, branched and branched circular polypeptides may be synthesized by non-translation natural process and by entirely synthetic methods, as well. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. In fact, blockage of the amino or carboxyl group in a polypeptide, or both, by a covalent modification, is common in naturally occurring and synthetic polypeptides and such modifications may be present in polypeptides of the present invention, as well. For instance, the amino terminal residue of polypeptides made in *E. coli*, prior to proteolytic processing, almost invariably will be N-formylmethionine.

Useful post-synthetic (and post-translational) modifications include conjugation to detectable labels, such as fluorophores. A wide variety of amine-reactive and thiol-reactive fluorophore derivatives have been synthesized that react under nondenaturing

conditions with N-terminal amino groups and epsilon amino groups of lysine residues, on the one hand, and with free thiol groups of cysteine residues, on the other.

Kits are available commercially that permit conjugation of proteins to a variety of amine-reactive or thiol-reactive fluorophores: Molecular Probes, Inc. (Eugene, OR, USA),
 5 *e.g.*, offers kits for conjugating proteins to Alexa Fluor 350, Alexa Fluor 430, Fluorescein-EX, Alexa Fluor 488, Oregon Green 488, Alexa Fluor 532, Alexa Fluor 546, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, and Texas Red-X.

A wide variety of other amine-reactive and thiol-reactive fluorophores are available commercially (Molecular Probes, Inc., Eugene, OR, USA), including Alexa
 10 Fluor® 350, Alexa Fluor® 488, Alexa Fluor® 532, Alexa Fluor® 546, Alexa Fluor® 568, Alexa Fluor® 594, Alexa Fluor® 647 (monoclonal antibody labeling kits available from Molecular Probes, Inc., Eugene, OR, USA), BODIPY dyes, such as BODIPY 493/503, BODIPY FL, BODIPY R6G, BODIPY 530/550, BODIPY TMR, BODIPY 558/568, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY
 15 TR, BODIPY 630/650, BODIPY 650/665, Cascade Blue, Cascade Yellow, Dansyl, lissamine rhodamine B, Marina Blue, Oregon Green 488, Oregon Green 514, Pacific Blue, rhodamine 6G, rhodamine green, rhodamine red, tetramethylrhodamine, Texas Red (available from Molecular Probes, Inc., Eugene, OR, USA).

The polypeptides of the present invention can also be conjugated to fluorophores,
 20 other proteins, and other macromolecules, using bifunctional linking reagents. Common homobifunctional reagents include, *e.g.*, APG, AEDP, BASED, BMB, BMDB, BMH, BMOE, BM[PEO]3, BM[PEO]4, BS3, BSOE, DFDNB, DMA, DMP, DMS, DPDPB, DSG, DSP (Lomant's Reagent), DSS, DST, DTBP, DTME, DTSSP, EGS, HBVS, Sulfo-BSOE, Sulfo-DST, Sulfo-EGS (all available from Pierce, Rockford, IL, USA);
 25 common heterobifunctional cross-linkers include ABH, AMAS, ANB-NOS, APDP, ASBA, BMAP, BMPH, BMPS, EDC, EMCA, EMCH, EMCS, KMUA, KMH, GMBS, LC-SMCC, LC-SPDP, MBS, M2C2H, MPBH, MSA, NHS-ASA, PDPH, PMPI, SADP, SAED, SAND, SANPAH, SASD, SATP, SBAP, SFAD, SIA, SIAB, SMCC, SMPB, SMPH, SMPT, SPDP, Sulfo-EMCS, Sulfo-GMBS, Sulfo-HSAB, Sulfo-KMUS,
 30 Sulfo-LC-SPDP, Sulfo-MBS, Sulfo-NHS-LC-ASA, Sulfo-SADP, Sulfo-SANPAH, Sulfo-SIAB, Sulfo-SMCC, Sulfo-SMPB, Sulfo-LC-SMPT, SVSB, TFCS (all available from Pierce, Rockford, IL, USA).

Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can be conjugated, using such cross-linking reagents, to fluorophores that are not amine- or thiol-reactive. Other labels that usefully can be conjugated to polypeptides of the present invention include radioactive labels, echosonographic contrast reagents, and MRI contrast agents.

Polypeptides of the present invention, including full length polypeptide, fragments and fusion proteins, can also usefully be conjugated using cross-linking agents to carrier proteins, such as KLH, bovine thyroglobulin, and even bovine serum albumin (BSA), to increase immunogenicity for raising anti-HSP antibodies.

Polypeptides of the present invention, including full length polypeptide, fragments and fusion proteins, can also usefully be conjugated to polyethylene glycol (PEG); PEGylation increases the serum half life of proteins administered intravenously for replacement therapy. Delgado *et al.*, *Crit. Rev. Ther. Drug Carrier Syst.* 9(3-4): 249-304 (1992); Scott *et al.*, *Curr. Pharm. Des.* 4(6): 423-38 (1998); DeSantis *et al.*, *Curr. Opin. Biotechnol.* 10(4): 324-30 (1999). PEG monomers can be attached to the protein directly or through a linker, with PEGylation using PEG monomers activated with tresyl chloride (2,2,2-trifluoroethanesulphonyl chloride) permitting direct attachment under mild conditions.

Polypeptides of the present invention are also inclusive of analogs of a polypeptide encoded by a nucleic acid molecule according to the instant invention. In a preferred embodiment, this polypeptide is a HSP. In a more preferred embodiment, this polypeptide is derived from a polypeptide having part or all of the amino acid sequence of SEQ ID NO: 410-611. Also preferred is an analog polypeptide comprising one or more substitutions of non-natural amino acids or non-native inter-residue bonds compared to the naturally occurring polypeptide. In one embodiment, the analog is structurally similar to a HSP, but one or more peptide linkages is replaced by a linkage selected from the group consisting of --CH₂NH--, --CH₂S--, --CH₂-CH₂--, --CH=CH--(cis and trans), --COCH₂--, --CH(OH)CH₂-- and --CH₂SO--. In another embodiment, the analog comprises substitution of one or more amino acids of a HSP with a D-amino acid of the same type or other non-natural amino acid in order to generate more stable peptides. D-amino acids can readily be incorporated during chemical peptide synthesis: peptides assembled from D-amino acids are more resistant to proteolytic attack; incorporation of D-amino acids can

also be used to confer specific three-dimensional conformations on the peptide. Other amino acid analogues commonly added during chemical synthesis include ornithine, norleucine, phosphorylated amino acids (typically phosphoserine, phosphothreonine, phosphotyrosine), L-malonyltyrosine, a non-hydrolyzable analog of phosphotyrosine (*see*,
5 *e.g.*, Kole *et al.*, *Biochem. Biophys. Res. Com.* 209: 817-821 (1995)), and various halogenated phenylalanine derivatives.

Non-natural amino acids can be incorporated during solid phase chemical synthesis or by recombinant techniques, although the former is typically more common. Solid phase chemical synthesis of peptides is well established in the art. Procedures are
10 described, *inter alia*, in Chan *et al.* (eds.), Fmoc Solid Phase Peptide Synthesis: A Practical Approach (Practical Approach Series), Oxford Univ. Press (March 2000); Jones, Amino Acid and Peptide Synthesis (Oxford Chemistry Primers, No 7), Oxford Univ. Press (1992); and Bodanszky, Principles of Peptide Synthesis (Springer Laboratory), Springer Verlag (1993).

15 Amino acid analogues having detectable labels are also usefully incorporated during synthesis to provide derivatives and analogs. Biotin, for example can be added using biotinoyl--(9-fluorenylmethoxycarbonyl)-L-lysine (Fmoc biocytin) (Molecular Probes, Eugene, OR, USA). Biotin can also be added enzymatically by incorporation into a fusion protein of a *E. coli* BirA substrate peptide. The Fmoc and *t*BOC derivatives of
20 dabcyl-L-lysine (Molecular Probes, Inc., Eugene, OR, USA) can be used to incorporate the dabcyl chromophore at selected sites in the peptide sequence during synthesis. The aminonaphthalene derivative EDANS, the most common fluorophore for pairing with the dabcyl quencher in fluorescence resonance energy transfer (FRET) systems, can be introduced during automated synthesis of peptides by using EDANS--Fmoc-L-glutamic
25 acid or the corresponding *t*BOC derivative (both from Molecular Probes, Inc., Eugene, OR, USA). Tetramethylrhodamine fluorophores can be incorporated during automated Fmoc synthesis of peptides using (Fmoc)--TMR-L-lysine (Molecular Probes, Inc. Eugene, OR, USA).

Other useful amino acid analogues that can be incorporated during chemical
30 synthesis include aspartic acid, glutamic acid, lysine, and tyrosine analogues having allyl side-chain protection (Applied Biosystems, Inc., Foster City, CA, USA); the allyl side chain permits synthesis of cyclic, branched-chain, sulfonated, glycosylated, and phosphorylated peptides.

A large number of other Fmoc-protected non-natural amino acid analogues capable of incorporation during chemical synthesis are available commercially, including, e.g., Fmoc-2-aminobicyclo[2.2.1]heptane-2-carboxylic acid, Fmoc-3-endo-aminobicyclo[2.2.1]heptane-2-endo-carboxylic acid, Fmoc-3-exo-aminobicyclo[2.2.1]heptane-2-exo-carboxylic acid, Fmoc-3-endo-amino-bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid, Fmoc-3-exo-amino-bicyclo[2.2.1]hept-5-ene-2-exo-carboxylic acid, Fmoc-cis-2-amino-1-cyclohexanecarboxylic acid, Fmoc-trans-2-amino-1-cyclohexanecarboxylic acid, Fmoc-1-amino-1-cyclopentanecarboxylic acid, Fmoc-cis-2-amino-1-cyclopentanecarboxylic acid, Fmoc-1-amino-1-cyclopropanecarboxylic acid, Fmoc-D-2-amino-4-(ethylthio)butyric acid, Fmoc-L-2-amino-4-(ethylthio)butyric acid, Fmoc-L-buthionine, Fmoc-S-methyl-L-Cysteine, Fmoc-2-aminobenzoic acid (anthranillic acid), Fmoc-3-aminobenzoic acid, Fmoc-4-aminobenzoic acid, Fmoc-2-aminobenzophenone-2'-carboxylic acid, Fmoc-N-(4-aminobenzoyl)- β -alanine, Fmoc-2-amino-4,5-dimethoxybenzoic acid, Fmoc-4-aminohippuric acid, Fmoc-2-amino-3-hydroxybenzoic acid, Fmoc-2-amino-5-hydroxybenzoic acid, Fmoc-3-amino-4-hydroxybenzoic acid, Fmoc-4-amino-3-hydroxybenzoic acid, Fmoc-4-amino-2-hydroxybenzoic acid, Fmoc-5-amino-2-hydroxybenzoic acid, Fmoc-2-amino-3-methoxybenzoic acid, Fmoc-4-amino-3-methoxybenzoic acid, Fmoc-2-amino-3-methylbenzoic acid, Fmoc-2-amino-5-methylbenzoic acid, Fmoc-2-amino-6-methylbenzoic acid, Fmoc-3-amino-2-methylbenzoic acid, Fmoc-3-amino-4-methylbenzoic acid, Fmoc-4-amino-3-methylbenzoic acid, Fmoc-3-amino-2-naphtoic acid, Fmoc-D,L-3-amino-3-phenylpropionic acid, Fmoc-L-Methyldopa, Fmoc-2-amino-4,6-dimethyl-3-pyridinecarboxylic acid, Fmoc-D,L-amino-2-thiophenacetic acid, Fmoc-4-(carboxymethyl)piperazine, Fmoc-4-carboxypiperazine, Fmoc-4-(carboxymethyl)homopiperazine, Fmoc-4-phenyl-4-piperidinecarboxylic acid, Fmoc-L-1,2,3,4-tetrahydronorharman-3-carboxylic acid, Fmoc-L-thiazolidine-4-carboxylic acid, all available from The Peptide Laboratory (Richmond, CA, USA).

Non-natural residues can also be added biosynthetically by engineering a suppressor tRNA, typically one that recognizes the UAG stop codon, by chemical aminoacylation with the desired unnatural amino acid. Conventional site-directed mutagenesis is used to introduce the chosen stop codon UAG at the site of interest in the protein gene. When the acylated suppressor tRNA and the mutant gene are combined in

an *in vitro* transcription/translation system, the unnatural amino acid is incorporated in response to the UAG codon to give a protein containing that amino acid at the specified position. Liu *et al.*, *Proc. Natl Acad. Sci. USA* 96(9): 4780-5 (1999); Wang *et al.*, *Science* 292(5516): 498-500 (2001).

5 *Fusion Proteins*

Another aspect of the present invention relates to the fusion of a polypeptide of the present invention to heterologous polypeptides. In a preferred embodiment, the polypeptide of the present invention is a HSP. In a more preferred embodiment, the polypeptide of the present invention that is fused to a heterologous polypeptide comprises
10 part or all of the amino acid sequence of SEQ ID NO: 410-611, or is a mutein, homologous polypeptide, analog or derivative thereof. In an even more preferred embodiment, the fusion protein is encoded by a nucleic acid molecule comprising all or part of the nucleic acid sequence of SEQ ID NO: 1-409, or comprises all or part of a nucleic acid sequence that selectively hybridizes or is homologous to a nucleic acid
15 molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409.

The fusion proteins of the present invention will include at least one fragment of a polypeptide of the present invention, which fragment is at least 6, typically at least 8, often at least 15, and usefully at least 16, 17, 18, 19, or 20 amino acids long. The fragment of the polypeptide of the present to be included in the fusion can usefully be at least 25
20 amino acids long, at least 50 amino acids long, and can be at least 75, 100, or even 150 amino acids long. Fusions that include the entirety of a polypeptide of the present invention have particular utility.

The heterologous polypeptide included within the fusion protein of the present invention is at least 6 amino acids in length, often at least 8 amino acids in length, and
25 preferably at least 15, 20, or 25 amino acids in length. Fusions that include larger polypeptides, such as the IgG Fc region, and even entire proteins (such as GFP chromophore-containing proteins) are particularly useful.

As described above in the description of vectors and expression vectors of the present invention, which discussion is incorporated here by reference in its entirety,
30 heterologous polypeptides to be included in the fusion proteins of the present invention can usefully include those designed to facilitate purification and/or visualization of recombinantly-expressed proteins. See, e.g., Ausubel, Chapter 16, (1992), *supra*.

Although purification tags can also be incorporated into fusions that are chemically synthesized, chemical synthesis typically provides sufficient purity that further purification by HPLC suffices; however, visualization tags as above described retain their utility even when the protein is produced by chemical synthesis, and when so included
5 render the fusion proteins of the present invention useful as directly detectable markers of the presence of a polypeptide of the invention.

As also discussed above, heterologous polypeptides to be included in the fusion proteins of the present invention can usefully include those that facilitate secretion of recombinantly expressed proteins into the periplasmic space or extracellular milieu for
10 prokaryotic hosts or into the culture medium for eukaryotic cells through incorporation of secretion signals and/or leader sequences. For example, a His⁶ tagged protein can be purified on a Ni affinity column and a GST fusion protein can be purified on a glutathione affinity column. Similarly, a fusion protein comprising the Fc domain of IgG can be purified on a Protein A or Protein G column and a fusion protein comprising an epitope
15 tag such as myc can be purified using an immunoaffinity column containing an anti-c-myc antibody. It is preferable that the epitope tag be separated from the protein encoded by the essential gene by an enzymatic cleavage site that can be cleaved after purification. See also the discussion of nucleic acid molecules encoding fusion proteins that may be expressed on the surface of a cell.

20 Other useful fusion proteins of the present invention include those that permit use of the polypeptide of the present invention as bait in a yeast two-hybrid system. See Bartel *et al.* (eds.), The Yeast Two-Hybrid System, Oxford University Press (1997); Zhu *et al.*, Yeast Hybrid Technologies, Eaton Publishing (2000); Fields *et al.*, *Trends Genet.* 10(8): 286-92 (1994); Mendelsohn *et al.*, *Curr. Opin. Biotechnol.* 5(5): 482-6 (1994);
25 Luban *et al.*, *Curr. Opin. Biotechnol.* 6(1): 59-64 (1995); Allen *et al.*, *Trends Biochem. Sci.* 20(12): 511-6 (1995); Drees, *Curr. Opin. Chem. Biol.* 3(1): 64-70 (1999); Topcu *et al.*, *Pharm. Res.* 17(9): 1049-55 (2000); Fashena *et al.*, *Gene* 250(1-2): 1-14 (2000); Colas *et al.*, *Nature* 380, 548-550 (1996); Norman, T. *et al.*, *Science* 285, 591-595 (1999); Fabbri *et al.*, *Oncogene* 18, 4357-4363 (1999); Xu *et al.*, *Proc Natl Acad Sci U S A.*
30 94, 12473-12478 (1997); Yang, *et al.*, *Nuc. Acids Res.* 23, 1152-1156 (1995); Kolonin *et al.*, *Proc Natl Acad Sci U S A* 95, 14266-14271 (1998); Cohen *et al.*, *Proc Natl Acad Sci U S A* 95, 14272-14277 (1998); Uetz, *et al.* *Nature* 403, 623-627(2000); Ito, *et al.*, *Proc Natl Acad Sci U S A* 98, 4569-4574 (2001). Typically, such fusion is to either *E. coli* LexA or

yeast GAL4 DNA binding domains. Related bait plasmids are available that express the bait fused to a nuclear localization signal.

Other useful fusion proteins include those that permit display of the encoded polypeptide on the surface of a phage or cell, fusions to intrinsically fluorescent proteins, such as green fluorescent protein (GFP), and fusions to the IgG Fc region, as described above.

The polypeptides of the present invention can also usefully be fused to protein toxins, such as *Pseudomonas* exotoxin A, diphtheria toxin, shiga toxin A, anthrax toxin lethal factor, ricin, in order to effect ablation of cells that bind or take up the proteins of the present invention.

Fusion partners include, *inter alia*, *myc*, hemagglutinin (HA), GST, immunoglobulins, β -galactosidase, biotin trpE, protein A, β -lactamase, α -amylase, maltose binding protein, alcohol dehydrogenase, polyhistidine (for example, six histidine at the amino and/or carboxyl terminus of the polypeptide), lacZ, green fluorescent protein (GFP), yeast α mating factor, GAL4 transcription activation or DNA binding domain, luciferase, and serum proteins such as ovalbumin, albumin and the constant domain of IgG. *See, e.g.*, Ausubel (1992), *supra* and Ausubel (1999), *supra*. Fusion proteins may also contain sites for specific enzymatic cleavage, such as a site that is recognized by enzymes such as Factor XIII, trypsin, pepsin, or any other enzyme known in the art. Fusion proteins will typically be made by either recombinant nucleic acid methods, as described above, chemically synthesized using techniques well known in the art (*e.g.*, a Merrifield synthesis), or produced by chemical cross-linking.

Another advantage of fusion proteins is that the epitope tag can be used to bind the fusion protein to a plate or column through an affinity linkage for screening binding proteins or other molecules that bind to the HSP.

As further described below, the polypeptides of the present invention can readily be used as specific immunogens to raise antibodies that specifically recognize polypeptides of the present invention including HSPs and their allelic variants and homologues. The antibodies, in turn, can be used, *inter alia*, specifically to assay for the polypeptides of the present invention, particularly HSPs, *e.g.* by ELISA for detection of protein fluid samples, such as serum, by immunohistochemistry or laser scanning cytometry, for detection of protein in tissue samples, or by flow cytometry, for detection of intracellular protein in cell suspensions, for specific antibody-mediated isolation and/or

purification of HSPs, as for example by immunoprecipitation, and for use as specific agonists or antagonists of HSPs.

One may determine whether polypeptides of the present invention including HSPs, muneins, homologous proteins or allelic variants or fusion proteins of the present invention
5 are functional by methods known in the art. For instance, residues that are tolerant of change while retaining function can be identified by altering the polypeptide at known residues using methods known in the art, such as alanine scanning mutagenesis, Cunningham *et al.*, *Science* 244(4908): 1081-5 (1989); transposon linker scanning mutagenesis, Chen *et al.*, *Gene* 263(1-2): 39-48 (2001); combinations of homolog- and
10 alanine-scanning mutagenesis, Jin *et al.*, *J. Mol. Biol.* 226(3): 851-65 (1992); combinatorial alanine scanning, Weiss *et al.*, *Proc. Natl. Acad. Sci USA* 97(16): 8950-4 (2000), followed by functional assay. Transposon linker scanning kits are available commercially (New England Biolabs, Beverly, MA, USA, catalog. no. E7-102S; EZ::TN™ In-Frame Linker Insertion Kit, catalogue no. EZI04KN, (Epicentre
15 Technologies Corporation, Madison, WI, USA).

Purification of the polypeptides or fusion proteins of the present invention is well known and within the skill of one having ordinary skill in the art. *See, e.g.*, Scopes, Protein Purification, 2d ed. (1987). Purification of recombinantly expressed polypeptides is described above. Purification of chemically-synthesized peptides can readily be
20 effected, *e.g.*, by HPLC.

Accordingly, it is an aspect of the present invention to provide the isolated polypeptides or fusion proteins of the present invention in pure or substantially pure form in the presence of absence of a stabilizing agent. Stabilizing agents include both proteinaceous and non-proteinaceous material and are well known in the art. Stabilizing
25 agents, such as albumin and polyethylene glycol (PEG) are known and are commercially available.

Although high levels of purity are preferred when the isolated polypeptide or fusion protein of the present invention are used as therapeutic agents, such as in vaccines and replacement therapy, the isolated polypeptides of the present invention are also useful
30 at lower purity. For example, partially purified polypeptides of the present invention can be used as immunogens to raise antibodies in laboratory animals.

In a preferred embodiment, the purified and substantially purified polypeptides of the present invention are in compositions that lack detectable ampholytes, acrylamide monomers, bis-acrylamide monomers, and polyacrylamide.

The polypeptides or fusion proteins of the present invention can usefully be
5 attached to a substrate. The substrate can be porous or solid, planar or non-planar; the bond can be covalent or noncovalent. For example, the peptides of the invention may be stabilized by covalent linkage to albumin. See, U.S. Patent No. 5,876,969, the contents of which are hereby incorporated in its entirety.

For example, the polypeptides or fusion proteins of the present invention can
10 usefully be bound to a porous substrate, commonly a membrane, typically comprising nitrocellulose, polyvinylidene fluoride (PVDF), or cationically derivatized, hydrophilic PVDF; so bound, the polypeptides or fusion proteins of the present invention can be used to detect and quantify antibodies, *e.g.* in serum, that bind specifically to the immobilized polypeptide or fusion protein of the present invention.

15 As another example, the polypeptides or fusion proteins of the present invention can usefully be bound to a substantially nonporous substrate, such as plastic, to detect and quantify antibodies, *e.g.* in serum, that bind specifically to the immobilized protein of the present invention. Such plastics include polymethylacrylic, polyethylene, polypropylene, polyacrylate, polymethylmethacrylate, polyvinylchloride, polytetrafluoroethylene,
20 polystyrene, polycarbonate, polyacetal, polysulfone, celluloseacetate, cellulosenitrate, nitrocellulose, or mixtures thereof; when the assay is performed in a standard microtiter dish, the plastic is typically polystyrene.

The polypeptides and fusion proteins of the present invention can also be attached to a substrate suitable for use as a surface enhanced laser desorption ionization source; so
25 attached, the polypeptide or fusion protein of the present invention is useful for binding and then detecting secondary proteins that bind with sufficient affinity or avidity to the surface-bound polypeptide or fusion protein to indicate biologic interaction there between. The polypeptides or fusion proteins of the present invention can also be attached to a substrate suitable for use in surface plasmon resonance detection; so attached, the
30 polypeptide or fusion protein of the present invention is useful for binding and then detecting secondary proteins that bind with sufficient affinity or avidity to the surface-bound polypeptide or fusion protein to indicate biological interaction there between.

Antibodies

In another aspect, the invention provides antibodies, including fragments and derivatives thereof, that bind specifically to polypeptides encoded by the nucleic acid molecules of the invention. In a preferred embodiment, the antibodies are specific for a polypeptide that is a HSP, or a fragment, mutein, derivative, analog or fusion protein thereof. In a more preferred embodiment, the antibodies are specific for a polypeptide that comprises SEQ ID NO: 410-611, or a fragment, mutein, derivative, analog or fusion protein thereof.

The antibodies of the present invention can be specific for linear epitopes, discontinuous epitopes, or conformational epitopes of such proteins or protein fragments, either as present on the protein in its native conformation or, in some cases, as present on the proteins as denatured, as, *e.g.*, by solubilization in SDS. New epitopes may be also due to a difference in post translational modifications (PTMs) in disease versus normal tissue. For example, a particular site on a HSP may be glycosylated in cancerous cells, but not glycosylated in normal cells or vis versa. In addition, alternative splice forms of a HSP may be indicative of cancer. Differential degradation of the C or N-terminus of a HSP may also be a marker or target for anticancer therapy. For example, an HSP may be N-terminal degraded in cancer cells exposing new epitopes to which antibodies may selectively bind for diagnostic or therapeutic uses.

As is well known in the art, the degree to which an antibody can discriminate among molecular species in a mixture will depend, in part, upon the conformational relatedness of the species in the mixture; typically, the antibodies of the present invention will discriminate over adventitious binding to non-HSP polypeptides by at least two-fold, more typically by at least 5-fold, typically by more than 10-fold, 25-fold, 50-fold, 75-fold, and often by more than 100-fold, and on occasion by more than 500-fold or 1000-fold. When used to detect the proteins or protein fragments of the present invention, the antibody of the present invention is sufficiently specific when it can be used to determine the presence of the polypeptide of the present invention in samples derived from human hepatic.

Typically, the affinity or avidity of an antibody (or antibody multimer, as in the case of an IgM pentamer) of the present invention for a protein or protein fragment of the present invention will be at least about 1×10^{-6} molar (M), typically at least about 5×10^{-7}

M, 1×10^{-7} M, with affinities and avidities of at least 1×10^{-8} M, 5×10^{-9} M, 1×10^{-10} M and up to 1×10^{-13} M proving especially useful.

The antibodies of the present invention can be naturally occurring forms, such as IgG, IgM, IgD, IgE, IgY, and IgA, from any avian, reptilian, or mammalian species.

5 Human antibodies can, but will infrequently, be drawn directly from human donors or human cells. In such case, antibodies to the polypeptides of the present invention will typically have resulted from fortuitous immunization, such as autoimmune immunization, with the polypeptide of the present invention. Such antibodies will typically, but will not invariably, be polyclonal. In addition, individual polyclonal antibodies may be isolated
10 and cloned to generate monoclonals.

Human antibodies are more frequently obtained using transgenic animals that express human immunoglobulin genes, which transgenic animals can be affirmatively immunized with the protein immunogen of the present invention. Human Ig-transgenic mice capable of producing human antibodies and methods of producing human antibodies
15 therefrom upon specific immunization are described, *inter alia*, in U.S. Patent Nos. 6,162,963; 6,150,584; 6,114,598; 6,075,181; 5,939,598; 5,877,397; 5,874,299; 5,814,318; 5,789,650; 5,770,429; 5,661,016; 5,633,425; 5,625,126; 5,569,825; 5,545,807; 5,545,806, and 5,591,669, the disclosures of which are incorporated herein by reference in their entireties. Such antibodies are typically monoclonal, and are typically produced using
20 techniques developed for production of murine antibodies.

Human antibodies are particularly useful, and often preferred, when the antibodies of the present invention are to be administered to human beings as *in vivo* diagnostic or therapeutic agents, since recipient immune response to the administered antibody will often be substantially less than that occasioned by administration of an antibody derived
25 from another species, such as mouse.

IgG, IgM, IgD, IgE, IgY, and IgA antibodies of the present invention are also usefully obtained from other species, including mammals such as rodents (typically mouse, but also rat, guinea pig, and hamster), lagomorphs (typically rabbits), and also larger mammals, such as sheep, goats, cows, and horses; or egg laying birds or reptiles
30 such as chickens or alligators. In such cases, as with the transgenic human-antibody-producing non-human mammals, fortuitous immunization is not required, and the non-human mammal is typically affirmatively immunized, according to standard immunization

protocols, with the polypeptide of the present invention. One form of avian antibodies may be generated using techniques described in WO 00/29444, published 25 May 2000.

As discussed above, virtually all fragments of 8 or more contiguous amino acids of a polypeptide of the present invention can be used effectively as immunogens when
5 conjugated to a carrier, typically a protein such as bovine thyroglobulin, keyhole limpet hemocyanin, or bovine serum albumin, conveniently using a bifunctional linker such as those described elsewhere above, which discussion is incorporated by reference here.

Immunogenicity can also be conferred by fusion of the polypeptide of the present invention to other moieties. For example, polypeptides of the present invention can be
10 produced by solid phase synthesis on a branched polylysine core matrix; these multiple antigenic peptides (MAPs) provide high purity, increased avidity, accurate chemical definition and improved safety in vaccine development. Tam *et al.*, *Proc. Natl. Acad. Sci. USA* 85: 5409-5413 (1988); Posnett *et al.*, *J. Biol. Chem.* 263: 1719-1725 (1988).

Protocols for immunizing non-human mammals or avian species are well-
15 established in the art. See Harlow *et al.* (eds.), Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory (1998); Coligan *et al.* (eds.), Current Protocols in Immunology, John Wiley & Sons, Inc. (2001); Zola, Monoclonal Antibodies: Preparation and Use of Monoclonal Antibodies and Engineered Antibody Derivatives (Basics: From Background to Bench), Springer Verlag (2000); Gross M, Speck *J.Dtsch. Tierarztl. Wochenschr.* 103: 417-422 (1996). Immunization protocols often include multiple
20 immunizations, either with or without adjuvants such as Freund's complete adjuvant and Freund's incomplete adjuvant, and may include naked DNA immunization (Moss, *Semin. Immunol.* 2: 317-327 (1990)).

Antibodies from non-human mammals and avian species can be polyclonal or
25 monoclonal, with polyclonal antibodies having certain advantages in immunohistochemical detection of the polypeptides of the present invention and monoclonal antibodies having advantages in identifying and distinguishing particular epitopes of the polypeptides of the present invention. Antibodies from avian species may have particular advantage in detection of the polypeptides of the present invention, in
30 human serum or tissues (Vikinge *et al.*, *Biosens. Bioelectron.* 13: 1257-1262 (1998). Following immunization, the antibodies of the present invention can be obtained using any art-accepted technique. Such techniques are well known in the art and are described in detail in references such as Coligan, *supra*; Zola, *supra*; Howard *et al.* (eds.), Basic

Methods in Antibody Production and Characterization, CRC Press (2000); Harlow, *supra*; Davis (ed.), Monoclonal Antibody Protocols, Vol. 45, Humana Press (1995); Delves (ed.), Antibody Production: Essential Techniques, John Wiley & Son Ltd (1997); and Kenney, Antibody Solution: An Antibody Methods Manual, Chapman & Hall (1997).

5 Briefly, such techniques include, *inter alia*, production of monoclonal antibodies by hybridomas and expression of antibodies or fragments or derivatives thereof from host cells engineered to express immunoglobulin genes or fragments thereof. These two methods of production are not mutually exclusive: genes encoding antibodies specific for the polypeptides of the present invention can be cloned from hybridomas and thereafter
10 expressed in other host cells. Nor need the two necessarily be performed together: *e.g.*, genes encoding antibodies specific for the polypeptides of the present invention can be cloned directly from B cells known to be specific for the desired protein, as further described in U.S. Patent No. 5,627,052, the disclosure of which is incorporated herein by reference in its entirety, or from antibody-displaying phage.

15 Recombinant expression in host cells is particularly useful when fragments or derivatives of the antibodies of the present invention are desired.

Host cells for recombinant antibody production of whole antibodies, antibody fragments, or antibody derivatives can be prokaryotic or eukaryotic.

20 Prokaryotic hosts are particularly useful for producing phage displayed antibodies of the present invention.

The technology of phage-displayed antibodies, in which antibody variable region fragments are fused, for example, to the gene III protein (pIII) or gene VIII protein (pVIII) for display on the surface of filamentous phage, such as M13, is by now well-established. *See, e.g.*, Sidhu, *Curr. Opin. Biotechnol.* 11(6): 610-6 (2000); Griffiths *et al.*, *Curr. Opin. Biotechnol.* 9(1): 102-8 (1998); Hoogenboom *et al.*, *Immunotechnology*, 4(1): 1-20 (1998);
25 Rader *et al.*, *Current Opinion in Biotechnology* 8: 503-508 (1997); Aujame *et al.*, *Human Antibodies* 8: 155-168 (1997); Hoogenboom, *Trends in Biotechnol.* 15: 62-70 (1997); de Kruif *et al.*, 17: 453-455 (1996); Barbas *et al.*, *Trends in Biotechnol.* 14: 230-234 (1996); Winter *et al.*, *Ann. Rev. Immunol.* 433-455 (1994). Techniques and protocols required to
30 generate, propagate, screen (pan), and use the antibody fragments from such libraries have recently been compiled. *See, e.g.*, Barbas (2001), *supra*; Kay, *supra*; and Abelson, *supra*.

Typically, phage-displayed antibody fragments are scFv fragments or Fab fragments; when desired, full length antibodies can be produced by cloning the variable

regions from the displaying phage into a complete antibody and expressing the full length antibody in a further prokaryotic or a eukaryotic host cell. Eukaryotic cells are also useful for expression of the antibodies, antibody fragments, and antibody derivatives of the present invention. For example, antibody fragments of the present invention can be
5 produced in *Pichia pastoris* and in *Saccharomyces cerevisiae*. See, e.g., Takahashi *et al.*, *Biosci. Biotechnol. Biochem.* 64(10): 2138-44 (2000); Freyre *et al.*, *J. Biotechnol.* 76(2-3):1 57-63 (2000); Fischer *et al.*, *Biotechnol. Appl. Biochem.* 30 (Pt 2): 117-20 (1999); Pennell *et al.*, *Res. Immunol.* 149(6): 599-603 (1998); Eldin *et al.*, *J. Immunol. Methods.* 201(1): 67-75 (1997);, Frenken *et al.*, *Res. Immunol.* 149(6): 589-99 (1998); and
10 Shusta *et al.*, *Nature Biotechnol.* 16(8): 773-7 (1998).

Antibodies, including antibody fragments and derivatives, of the present invention can also be produced in insect cells. See, e.g., Li *et al.*, *Protein Expr. Purif.* 21(1): 121-8 (2001); Ailor *et al.*, *Biotechnol. Bioeng.* 58(2-3): 196-203 (1998); Hsu *et al.*, *Biotechnol. Prog.* 13(1): 96-104 (1997); Edelman *et al.*, *Immunology* 91(1): 13-9 (1997); and Nesbit *et al.*, *J. Immunol. Methods* 151(1-2): 201-8 (1992).
15

Antibodies and fragments and derivatives thereof of the present invention can also be produced in plant cells, particularly maize or tobacco, Giddings *et al.*, *Nature Biotechnol.* 18(11): 1151-5 (2000); Gavilondo *et al.*, *Biotechniques* 29(1): 128-38 (2000); Fischer *et al.*, *J. Biol. Regul. Homeost. Agents* 14(2): 83-92 (2000); Fischer *et al.*,
20 *Biotechnol. Appl. Biochem.* 30 (Pt 2): 113-6 (1999); Fischer *et al.*, *Biol. Chem.* 380(7-8): 825-39 (1999); Russell, *Curr. Top. Microbiol. Immunol.* 240: 119-38 (1999); and Ma *et al.*, *Plant Physiol.* 109(2): 341-6 (1995).

Antibodies, including antibody fragments and derivatives, of the present invention can also be produced in transgenic, non-human, mammalian milk. See, e.g. Pollock *et al.*,
25 *J. Immunol Methods.* 231: 147-57 (1999); Young *et al.*, *Res. Immunol.* 149: 609-10 (1998); and Limonta *et al.*, *Immunotechnology* 1: 107-13 (1995).

Mammalian cells useful for recombinant expression of antibodies, antibody fragments, and antibody derivatives of the present invention include CHO cells, COS cells, 293 cells, and myeloma cells. Verma *et al.*, *J. Immunol. Methods* 216(1-2):165-81
30 (1998) review and compare bacterial, yeast, insect and mammalian expression systems for expression of antibodies. Antibodies of the present invention can also be prepared by cell free translation, as further described in Merk *et al.*, *J. Biochem. (Tokyo)* 125(2): 328-33 (1999) and Ryabova *et al.*, *Nature Biotechnol.* 15(1): 79-84 (1997), and in the milk of

transgenic animals, as further described in Pollock *et al.*, *J. Immunol. Methods* 231(1-2): 147-57 (1999).

The invention further provides antibody fragments that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention. Among such useful fragments are Fab, Fab', Fv, F(ab')₂, and single chain Fv (scFv) fragments. Other useful fragments are described in Hudson, *Curr. Opin. Biotechnol.* 9(4): 395-402 (1998).

The present invention also relates to antibody derivatives that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention.

Among such useful derivatives are chimeric, primatized, and humanized antibodies; such derivatives are less immunogenic in human beings, and thus are more suitable for *in vivo* administration, than are unmodified antibodies from non-human mammalian species. Another useful method is PEGylation to increase the serum half life of the antibodies.

Chimeric antibodies typically include heavy and/or light chain variable regions (including both CDR and framework residues) of immunoglobulins of one species, typically mouse, fused to constant regions of another species, typically human. *See, e.g.*, Morrison *et al.*, *Proc. Natl. Acad. Sci USA* 81(21): 6851-5 (1984); Sharon *et al.*, *Nature* 309(5966): 364-7 (1984); Takeda *et al.*, *Nature* 314(6010): 452-4 (1985); and U.S. Patent No. 5,807,715 the disclosure of which is incorporated herein by reference in its entirety. Primatized and humanized antibodies typically include heavy and/or light chain CDRs from a murine antibody grafted into a non-human primate or human antibody V region framework, usually further comprising a human constant region, Riechmann *et al.*, *Nature* 332(6162): 323-7 (1988); Co *et al.*, *Nature* 351(6326): 501-2 (1991); and U.S. Patent Nos. 6,054,297; 5,821,337; 5,770,196; 5,766,886; 5,821,123; 5,869,619; 6,180,377; 6,013,256; 5,693,761; and 6,180,370, the disclosures of which are incorporated herein by reference in

their entireties. Other useful antibody derivatives of the invention include heteromeric antibody complexes and antibody fusions, such as diabodies (bispecific antibodies), single-chain diabodies, and intrabodies.

It is contemplated that the nucleic acids encoding the antibodies of the present invention can be operably joined to other nucleic acids forming a recombinant vector for cloning or for expression of the antibodies of the invention. Accordingly, the present invention includes any recombinant vector containing the coding sequences, or part thereof, whether for eukaryotic transduction, transfection or gene therapy. Such vectors may be prepared using conventional molecular biology techniques, known to those with skill in the art, and would comprise DNA encoding sequences for the immunoglobulin V-regions including framework and CDRs or parts thereof, and a suitable promoter either with or without a signal sequence for intracellular transport. Such vectors may be transduced or transfected into eukaryotic cells or used for gene therapy (Marasco et al., *Proc. Natl. Acad. Sci. (USA)* 90: 7889-7893 (1993); Duan et al., *Proc. Natl. Acad. Sci. (USA)* 91: 5075-5079 (1994), by conventional techniques, known to those with skill in the art.

The antibodies of the present invention, including fragments and derivatives thereof, can usefully be labeled. It is, therefore, another aspect of the present invention to provide labeled antibodies that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention. The choice of label depends, in part, upon the desired use.

For example, when the antibodies of the present invention are used for immunohistochemical staining of tissue samples, the label can usefully be an enzyme that catalyzes production and local deposition of a detectable product. Enzymes typically conjugated to antibodies to permit their immunohistochemical visualization are well known, and include alkaline phosphatase, β -galactosidase, glucose oxidase, horseradish peroxidase (HRP), and urease. Typical substrates for production and deposition of visually detectable products include o-nitrophenyl-beta-D-galactopyranoside (ONPG); o-phenylenediamine dihydrochloride (OPD); p-nitrophenyl phosphate (PNPP); p-nitrophenyl-beta-D-galactopyranoside (PNPG); 3',3'-diaminobenzidine (DAB); 3-amino-

9-ethylcarbazole (AEC); 4-chloro-1-naphthol (CN);
5-bromo-4-chloro-3-indolyl-phosphate (BCIP); ABTS®; BluoGal; iodonitrotetrazolium
(INT); nitroblue tetrazolium chloride (NBT); phenazine methosulfate (PMS);
phenolphthalein monophosphate (PMP); tetramethyl benzidine (TMB); tetranitroblue
5 tetrazolium (TNBT); X-Gal; X-Gluc; and X-Glucoside.

Other substrates can be used to produce products for local deposition that are
luminescent. For example, in the presence of hydrogen peroxide (H₂O₂), horseradish
peroxidase (HRP) can catalyze the oxidation of cyclic diacylhydrazides, such as luminol.
Immediately following the oxidation, the luminol is in an excited state (intermediate
10 reaction product), which decays to the ground state by emitting light. Strong enhancement
of the light emission is produced by enhancers, such as phenolic compounds. Advantages
include high sensitivity, high resolution, and rapid detection without radioactivity and
requiring only small amounts of antibody. *See, e.g., Thorpe et al., Methods Enzymol.* 133:
331-53 (1986); Kricka *et al., J. Immunoassay* 17(1): 67-83 (1996); and Lundqvist *et al., J.*
15 *Biolumin. Chemilumin.* 10(6): 353-9 (1995). Kits for such enhanced chemiluminescent
detection (ECL) are available commercially. The antibodies can also be labeled using
colloidal gold.

As another example, when the antibodies of the present invention are used, *e.g., for*
flow cytometric detection, for scanning laser cytometric detection, or for fluorescent
20 immunoassay, they can usefully be labeled with fluorophores. There are a wide variety of
fluorophore labels that can usefully be attached to the antibodies of the present invention.
For flow cytometric applications, both for extracellular detection and for intracellular
detection, common useful fluorophores can be fluorescein isothiocyanate (FITC),
allophycocyanin (APC), R-phycoerythrin (PE), peridinin chlorophyll protein (PerCP),
25 Texas Red, Cy3, Cy5, fluorescence resonance energy tandem fluorophores such as PerCP-
Cy5.5, PE-Cy5, PE-Cy5.5, PE-Cy7, PE-Texas Red, and APC-Cy7.

Other fluorophores include, *inter alia*, Alexa Fluor® 350, Alexa Fluor® 488,
Alexa Fluor® 532, Alexa Fluor® 546, Alexa Fluor® 568, Alexa Fluor® 594, Alexa
Fluor® 647 (monoclonal antibody labeling kits available from Molecular Probes, Inc.,
30 Eugene, OR, USA), BODIPY dyes, such as BODIPY 493/503, BODIPY FL, BODIPY
R6G, BODIPY 530/550, BODIPY TMR, BODIPY 558/568, BODIPY 558/568, BODIPY
564/570, BODIPY 576/589, BODIPY 581/591, BODIPY TR, BODIPY 630/650,
BODIPY 650/665, Cascade Blue, Cascade Yellow, Dansyl, lissamine rhodamine B,

Marina Blue, Oregon Green 488, Oregon Green 514, Pacific Blue, rhodamine 6G, rhodamine green, rhodamine red, tetramethylrhodamine, Texas Red (available from Molecular Probes, Inc., Eugene, OR, USA), and Cy2, Cy3, Cy3.5, Cy5, Cy5.5, Cy7, all of which are also useful for fluorescently labeling the antibodies of the present invention.

- 5 For secondary detection using labeled avidin, streptavidin, captavidin or neutravidin, the antibodies of the present invention can usefully be labeled with biotin.

When the antibodies of the present invention are used, *e.g.*, for western blotting applications, they can usefully be labeled with radioisotopes, such as ^{33}P , ^{32}P , ^{35}S , ^3H , and ^{125}I . As another example, when the antibodies of the present invention are used for
10 radioimmunoassay, the label can usefully be ^{228}Th , ^{227}Ac , ^{225}Ac , ^{223}Ra , ^{213}Bi , ^{212}Pb , ^{212}Bi , ^{211}At , ^{203}Pb , ^{194}Os , ^{188}Re , ^{186}Re , ^{153}Sm , ^{149}Tb , ^{131}I , ^{125}I , ^{111}In , ^{105}Rh , $^{99\text{m}}\text{Tc}$, ^{97}Ru , ^{90}Y , ^{90}Sr , ^{88}Y , ^{72}Se , ^{67}Cu , or ^{47}Sc .

As another example, when the antibodies of the present invention are to be used for *in vivo* diagnostic use, they can be rendered detectable by conjugation to MRI contrast
15 agents, such as gadolinium diethylenetriaminepentaacetic acid (DTPA), Lauffer *et al.*, *Radiology* 207(2): 529-38 (1998), or by radioisotopic labeling.

As would be understood, use of the labels described above is not restricted to the application as for which they were mentioned.

The antibodies of the present invention, including fragments and derivatives
20 thereof, can also be conjugated to toxins, in order to target the toxin's ablative action to cells that display and/or express the polypeptides of the present invention. Commonly, the antibody in such immunotoxins is conjugated to Pseudomonas exotoxin A, diphtheria toxin, shiga toxin A, anthrax toxin lethal factor, or ricin. See Hall (ed.), Immunotoxin Methods and Protocols (Methods in Molecular Biology, vol. 166), Humana Press (2000);
25 and Frankel *et al.* (eds.), Clinical Applications of Immunotoxins, Springer-Verlag (1998).

The antibodies of the present invention can usefully be attached to a substrate, and it is, therefore, another aspect of the invention to provide antibodies that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or
30 the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, attached to a substrate. Substrates can be porous or nonporous, planar or nonplanar. For example, the antibodies of the present invention

can usefully be conjugated to filtration media, such as NHS-activated Sepharose or CNBr-activated Sepharose for purposes of immunoaffinity chromatography. For example, the antibodies of the present invention can usefully be attached to paramagnetic microspheres, typically by biotin-streptavidin interaction, which microsphere can then be used for isolation of cells that express or display the polypeptides of the present invention. As another example, the antibodies of the present invention can usefully be attached to the surface of a microtiter plate for ELISA.

As noted above, the antibodies of the present invention can be produced in prokaryotic and eukaryotic cells. It is, therefore, another aspect of the present invention to provide cells that express the antibodies of the present invention, including hybridoma cells, B cells, plasma cells, and host cells recombinantly modified to express the antibodies of the present invention.

In yet a further aspect, the present invention provides aptamers evolved to bind specifically to one or more of the HSPs of the present invention or to polypeptides encoded by the HSNAs of the invention.

In sum, one of skill in the art, provided with the teachings of this invention, has available a variety of methods which may be used to alter the biological properties of the antibodies of this invention including methods which would increase or decrease the stability or half-life, immunogenicity, toxicity, affinity or yield of a given antibody molecule, or to alter it in any other way that may render it more suitable for a particular application.

Transgenic Animals and Cells

In another aspect, the invention provides transgenic cells and non-human organisms comprising nucleic acid molecules of the invention. In a preferred embodiment, the transgenic cells and non-human organisms comprise a nucleic acid molecule encoding a HSP. In a preferred embodiment, the HSP comprises an amino acid sequence selected from SEQ ID NO: 410-611, or a fragment, mutein, homologous protein or allelic variant thereof. In another preferred embodiment, the transgenic cells and non-human organism comprise a HSNA of the invention, preferably a HSNA comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-409, or a part, substantially similar nucleic acid molecule, allelic variant or hybridizing nucleic acid molecule thereof.

In another embodiment, the transgenic cells and non-human organisms have a targeted disruption or replacement of the endogenous orthologue of the human HSG. The transgenic cells can be embryonic stem cells or somatic cells. The transgenic non-human organisms can be chimeric, nonchimeric heterozygotes, and nonchimeric homozygotes.

5 Methods of producing transgenic animals are well known in the art. *See, e.g., Hogan et al., Manipulating the Mouse Embryo: A Laboratory Manual, 2d ed., Cold Spring Harbor Press (1999); Jackson et al., Mouse Genetics and Transgenics: A Practical Approach, Oxford University Press (2000); and Pinkert, Transgenic Animal Technology: A Laboratory Handbook, Academic Press (1999).*

10 Any technique known in the art may be used to introduce a nucleic acid molecule of the invention into an animal to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection. (*see, e.g., Paterson et al., Appl. Microbiol. Biotechnol. 40: 691-698 (1994); Carver et al., Biotechnology 11: 1263-1270 (1993); Wright et al., Biotechnology 9: 830-834 (1991); and U.S. Patent No.*
15 *4,873,191, herein incorporated by reference in its entirety*); retrovirus-mediated gene transfer into germ lines, blastocysts or embryos (*see, e.g., Van der Putten et al., Proc. Natl. Acad. Sci., USA 82: 6148-6152 (1985)*); gene targeting in embryonic stem cells (*see, e.g., Thompson et al., Cell 56: 313-321 (1989)*); electroporation of cells or embryos (*see, e.g., Lo, 1983, Mol. Cell. Biol. 3: 1803-1814 (1983)*); introduction using a gene gun (*see,*
20 *e.g., Ulmer et al., Science 259: 1745-49 (1993)*); introducing nucleic acid constructs into embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (*see, e.g., Lavitrano et al., Cell 57: 717-723 (1989)*).

Other techniques include, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (*see, e.g.,*
25 *Campbell et al., Nature 380: 64-66 (1996); Wilmut et al., Nature 385: 810-813 (1997)*). The present invention provides for transgenic animals that carry the transgene (*i.e., a nucleic acid molecule of the invention*) in all their cells, as well as animals which carry the transgene in some, but not all their cells, *i.e. e., mosaic animals or chimeric animals.*

The transgene may be integrated as a single transgene or as multiple copies, such
30 as in concatamers, *e. g., head-to-head tandems or head-to-tail tandems.* The transgene may also be selectively introduced into and activated in a particular cell type by following, *e.g., the teaching of Lasko et al. et al., Proc. Natl. Acad. Sci. USA 89: 6232- 6236 (1992).*

The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished
5 by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR (RT-PCR).
10 Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding
15 strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to
20 both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited
25 to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Methods for creating a transgenic animal with a disruption of a targeted gene are
30 also well known in the art. In general, a vector is designed to comprise some nucleotide sequences homologous to the endogenous targeted gene. The vector is introduced into a cell so that it may integrate, via homologous recombination with chromosomal sequences, into the endogenous gene, thereby disrupting the function of the endogenous gene. The

transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type. *See, e.g., Gu et al., Science* 265: 103-106 (1994). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. *See, e.g., Smithies et al., Nature* 317: 230-234 (1985); Thomas *et al., Cell* 51: 503-512 (1987); Thompson *et al., Cell* 5: 313-321 (1989).

In one embodiment, a mutant, non-functional nucleic acid molecule of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous nucleic acid sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene. *See, e.g., Thomas, supra* and Thompson, *supra*. However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (*e.g., knockouts*) are administered to a patient in vivo. Such cells may be obtained from an animal or patient or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (*e.g., lymphocytes*), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, *e.g., by transduction* (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc.

The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, *e.g.*, in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, *e.g.*, genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. *See, e.g.*, U.S. Patent Nos. 5,399,349 and 5,460,959, each of which is incorporated by reference herein in its entirety.

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Computer Readable Means

A further aspect of the invention is a computer readable means for storing the nucleic acid and amino acid sequences of the instant invention. In a preferred embodiment, the invention provides a computer readable means for storing SEQ ID NO: 410-611 and SEQ ID NO: 1-409 as described herein, as the complete set of sequences or in any combination. The records of the computer readable means can be accessed for reading and display and for interface with a computer system for the application of programs allowing for the location of data upon a query for data meeting certain criteria, the comparison of sequences, the alignment or ordering of sequences meeting a set of criteria, and the like.

The nucleic acid and amino acid sequences of the invention are particularly useful as components in databases useful for search analyses as well as in sequence analysis algorithms. As used herein, the terms "nucleic acid sequences of the invention" and "amino acid sequences of the invention" mean any detectable chemical or physical
5 characteristic of a polynucleotide or polypeptide of the invention that is or may be reduced to or stored in a computer readable form. These include, without limitation, chromatographic scan data or peak data, photographic data or scan data therefrom, and mass spectrographic data.

This invention provides computer readable media having stored thereon sequences
10 of the invention. A computer readable medium may comprise one or more of the following: a nucleic acid sequence comprising a sequence of a nucleic acid sequence of the invention; an amino acid sequence comprising an amino acid sequence of the invention; a set of nucleic acid sequences wherein at least one of said sequences comprises the sequence of a nucleic acid sequence of the invention; a set of amino acid sequences
15 wherein at least one of said sequences comprises the sequence of an amino acid sequence of the invention; a data set representing a nucleic acid sequence comprising the sequence of one or more nucleic acid sequences of the invention; a data set representing a nucleic acid sequence encoding an amino acid sequence comprising the sequence of an amino acid sequence of the invention; a set of nucleic acid sequences wherein at least one of said
20 sequences comprises the sequence of a nucleic acid sequence of the invention; a set of amino acid sequences wherein at least one of said sequences comprises the sequence of an amino acid sequence of the invention; a data set representing a nucleic acid sequence comprising the sequence of a nucleic acid sequence of the invention; a data set representing a nucleic acid sequence encoding an amino acid sequence comprising the
25 sequence of an amino acid sequence of the invention. The computer readable medium can be any composition of matter used to store information or data, including, for example, commercially available floppy disks, tapes, hard drives, compact disks, and video disks.

Also provided by the invention are methods for the analysis of character sequences, particularly genetic sequences. Preferred methods of sequence analysis
30 include, for example, methods of sequence homology analysis, such as identity and similarity analysis, RNA structure analysis, sequence assembly, cladistic analysis, sequence motif analysis, open reading frame determination, nucleic acid base calling, and sequencing chromatogram peak analysis.

A computer-based method is provided for performing nucleic acid sequence identity or similarity identification. This method comprises the steps of providing a nucleic acid sequence comprising the sequence of a nucleic acid of the invention in a computer readable medium; and comparing said nucleic acid sequence to at least one
5 nucleic acid or amino acid sequence to identify sequence identity or similarity.

A computer-based method is also provided for performing amino acid homology identification, said method comprising the steps of: providing an amino acid sequence comprising the sequence of an amino acid of the invention in a computer readable medium; and comparing said amino acid sequence to at least one nucleic acid or an amino
10 acid sequence to identify homology.

A computer-based method is still further provided for assembly of overlapping nucleic acid sequences into a single nucleic acid sequence, said method comprising the steps of: providing a first nucleic acid sequence comprising the sequence of a nucleic acid of the invention in a computer readable medium; and screening for at least one
15 overlapping region between said first nucleic acid sequence and a second nucleic acid sequence. In addition, the invention includes a method of using patterns of expression associated with either the nucleic acids or proteins in a computer-based method to diagnose disease.

Diagnostic Methods for hepatic Cancer

20 The present invention also relates to quantitative and qualitative diagnostic assays and methods for detecting, diagnosing, monitoring, staging and predicting cancers by comparing expression of a HSNA or a HSP in a human patient that has or may have hepatic cancer, or who is at risk of developing hepatic cancer, with the expression of a HSNA or a HSP in a normal human control. For purposes of the present invention,
25 “expression of a HSNA” or “HSNA expression” means the quantity of HSNA mRNA that can be measured by any method known in the art or the level of transcription that can be measured by any method known in the art in a cell, tissue, organ or whole patient. Similarly, the term “expression of a HSP” or “HSP expression” means the amount of HSP that can be measured by any method known in the art or the level of translation of a
30 HSNA that can be measured by any method known in the art.

The present invention provides methods for diagnosing hepatic cancer in a patient, by analyzing for changes in levels of HSNA or HSP in cells, tissues, organs or bodily

fluids compared with levels of HSNA or HSP in cells, tissues, organs or bodily fluids of preferably the same type from a normal human control, wherein an increase, or decrease in certain cases, in levels of a HSNA or HSP in the patient versus the normal human control is associated with the presence of hepatic cancer or with a predilection to the disease. In
5 another preferred embodiment, the present invention provides methods for diagnosing hepatic cancer in a patient by analyzing changes in the structure of the mRNA of a HSG compared to the mRNA from a normal control. These changes include, without limitation, aberrant splicing, alterations in polyadenylation and/or alterations in 5' nucleotide capping. In yet another preferred embodiment, the present invention provides methods for
10 diagnosing hepatic cancer in a patient by analyzing changes in a HSP compared to a HSP from a normal patient. These changes include, *e.g.*, alterations, including post translational modifications such as glycosylation and/or phosphorylation of the HSP or changes in the subcellular HSP localization.

For purposes of the present invention, diagnosing means that HSNA or HSP levels
15 are used to determine the presence or absence of disease in a patient. As will be understood by those of skill in the art, measurement of other diagnostic parameters may be required for definitive diagnosis or determination of the appropriate treatment for the disease. The determination may be made by a clinician, a doctor, a testing laboratory, or a patient using an over the counter test. The patient may have symptoms of disease or may
20 be asymptomatic. In addition, the HSNA or HSP levels of the present invention may be used as screening marker to determine whether further tests or biopsies are warranted. In addition, the HSNA or HSP levels may be used to determine the vulnerability or susceptibility to disease.

In a preferred embodiment, the expression of a HSNA is measured by determining
25 the amount of a mRNA that encodes an amino acid sequence selected from SEQ ID NO: 410-611, a homolog, an allelic variant, or a fragment thereof. In a more preferred embodiment, the HSNA expression that is measured is the level of expression of a HSNA mRNA selected from SEQ ID NO: 1-409, or a hybridizing nucleic acid, homologous nucleic acid or allelic variant thereof, or a part of any of these nucleic acid molecules.
30 HSNA expression may be measured by any method known in the art, such as those described *supra*, including measuring mRNA expression by Northern blot, quantitative or qualitative reverse transcriptase PCR (RT-PCR), microarray, dot or slot blots or *in situ* hybridization. *See, e.g.*, Ausubel (1992), *supra*; Ausubel (1999), *supra*; Sambrook

(1989), *supra*; and Sambrook (2001), *supra*. HSNA transcription may be measured by any method known in the art including using a reporter gene hooked up to the promoter of a HSG of interest or doing nuclear run-off assays. Alterations in mRNA structure, *e.g.*, aberrant splicing variants, may be determined by any method known in the art, including, RT-PCR followed by sequencing or restriction analysis. As necessary, HSNA expression may be compared to a known control, such as normal hepatic nucleic acid, to detect a change in expression.

In another preferred embodiment, the expression of a HSP is measured by determining the level of a HSP having an amino acid sequence selected from the group consisting of SEQ ID NO: 410-611, a homolog, an allelic variant, or a fragment thereof. Such levels are preferably determined in at least one of cells, tissues, organs and/or bodily fluids, including determination of normal and abnormal levels. Thus, for instance, a diagnostic assay in accordance with the invention for diagnosing over- or underexpression of a HSNA or HSP compared to normal control bodily fluids, cells, or tissue samples may be used to diagnose the presence of hepatic cancer. The expression level of a HSP may be determined by any method known in the art, such as those described *supra*. In a preferred embodiment, the HSP expression level may be determined by radioimmunoassays, competitive-binding assays, ELISA, Western blot, FACS, immunohistochemistry, immunoprecipitation, proteomic approaches: two-dimensional gel electrophoresis (2D electrophoresis) and non-gel-based approaches such as mass spectrometry or protein interaction profiling. *See, e.g.*, Harlow (1999), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), *supra*. Alterations in the HSP structure may be determined by any method known in the art, including, *e.g.*, using antibodies that specifically recognize phosphoserine, phosphothreonine or phosphotyrosine residues, two-dimensional polyacrylamide gel electrophoresis (2D PAGE) and/or chemical analysis of amino acid residues of the protein. *Id.*

In a preferred embodiment, a radioimmunoassay (RIA) or an ELISA is used. An antibody specific to a HSP is prepared if one is not already available. In a preferred embodiment, the antibody is a monoclonal antibody. The anti-HSP antibody is bound to a solid support and any free protein binding sites on the solid support are blocked with a protein such as bovine serum albumin. A sample of interest is incubated with the antibody on the solid support under conditions in which the HSP will bind to the anti-HSP antibody. The sample is removed, the solid support is washed to remove unbound material, and an

anti-HSP antibody that is linked to a detectable reagent (a radioactive substance for RIA and an enzyme for ELISA) is added to the solid support and incubated under conditions in which binding of the HSP to the labeled antibody will occur. After binding, the unbound labeled antibody is removed by washing. For an ELISA, one or more substrates are added to produce a colored reaction product that is based upon the amount of an HSP in the sample. For an RIA, the solid support is counted for radioactive decay signals by any method known in the art. Quantitative results for both RIA and ELISA typically are obtained by reference to a standard curve.

Other methods to measure HSP levels are known in the art. For instance, a competition assay may be employed wherein an anti-HSP antibody is attached to a solid support and an allocated amount of a labeled HSP and a sample of interest are incubated with the solid support. The amount of labeled HSP attached to the solid support can be correlated to the quantity of a HSP in the sample.

Of the proteomic approaches, 2D PAGE is a well known technique. Isolation of individual proteins from a sample such as serum is accomplished using sequential separation of proteins by isoelectric point and molecular weight. Typically, polypeptides are first separated by isoelectric point (the first dimension) and then separated by size using an electric current (the second dimension). In general, the second dimension is perpendicular to the first dimension. Because no two proteins with different sequences are identical on the basis of both size and charge, the result of 2D PAGE is a roughly square gel in which each protein occupies a unique spot. Analysis of the spots with chemical or antibody probes, or subsequent protein microsequencing can reveal the relative abundance of a given protein and the identity of the proteins in the sample.

Expression levels of a HSNA can be determined by any method known in the art, including PCR and other nucleic acid methods, such as ligase chain reaction (LCR) and nucleic acid sequence based amplification (NASBA), can be used to detect malignant cells for diagnosis and monitoring of various malignancies. For example, reverse-transcriptase PCR (RT-PCR) is a powerful technique which can be used to detect the presence of a specific mRNA population in a complex mixture of thousands of other mRNA species. In RT-PCR, an mRNA species is first reverse transcribed to complementary DNA (cDNA) with use of the enzyme reverse transcriptase; the cDNA is then amplified as in a standard PCR reaction.

Hybridization to specific DNA molecules (*e.g.*, oligonucleotides) arrayed on a solid support can be used to both detect the expression of and quantitate the level of expression of one or more HSNAs of interest. In this approach, all or a portion of one or more HSNAs is fixed to a substrate. A sample of interest, which may comprise RNA, *e.g.*,
5 total RNA or polyA-selected mRNA, or a complementary DNA (cDNA) copy of the RNA is incubated with the solid support under conditions in which hybridization will occur between the DNA on the solid support and the nucleic acid molecules in the sample of interest. Hybridization between the substrate-bound DNA and the nucleic acid molecules in the sample can be detected and quantitated by several means, including, without
10 limitation, radioactive labeling or fluorescent labeling of the nucleic acid molecule or a secondary molecule designed to detect the hybrid.

The above tests can be carried out on samples derived from a variety of cells, bodily fluids and/or tissue extracts such as homogenates or solubilized tissue obtained from a patient. Tissue extracts are obtained routinely from tissue biopsy and autopsy
15 material. Bodily fluids useful in the present invention include blood, urine, saliva or any other bodily secretion or derivative thereof. As used herein "blood" includes whole blood, plasma, serum, circulating epithelial cells, constituents, or any derivative of blood.

In addition to detection in bodily fluids, the proteins and nucleic acids of the invention are suitable to detection by cell capture technology. Whole cells may be
20 captured by a variety of methods for example magnetic separation, U.S. Patent Nos. 5,200,084; 5,186,827; 5,108,933; 4,925,788, the disclosures of which are incorporated herein by reference in their entireties. Epithelial cells may be captured using such products as Dynabeads® or CELLection™ (DynaL Biotech, Oslo, Norway). Alternatively, fractions of blood may be captured, *e.g.*, the buffy coat fraction (50mm cells isolated from
25 5ml of blood) containing epithelial cells. In addition, cancer cells may be captured using the techniques described in WO 00/47998, the disclosure of which is incorporated herein by reference in its entirety. Once the cells are captured or concentrated, the proteins or nucleic acids are detected by the means described in the subject application. Alternatively, nucleic acids may be captured directly from blood samples, see U.S. Patent Nos.
30 6,156,504, 5,501,963; or WO 01/42504, the disclosures of which are incorporated herein by reference in their entireties.

In a preferred embodiment, the specimen tested for expression of HSNA or HSP includes without limitation hepatic tissue, hepatic cells grown in cell culture, blood,

serum, lymph node tissue, and lymphatic fluid. In another preferred embodiment, especially when metastasis of a primary hepatic cancer is known or suspected, specimens include, without limitation, tissues from brain, bone, bone marrow, liver, lungs, colon, and adrenal glands. In general, the tissues may be sampled by biopsy, including, without
5 limitation, needle biopsy, *e.g.*, transthoracic needle aspiration, cervical mediastinoscopy, endoscopic lymph node biopsy, video-assisted thoracoscopy, exploratory thoracotomy, bone marrow biopsy and bone marrow aspiration.

All the methods of the present invention may optionally include determining the expression levels of one or more other cancer markers in addition to determining the
10 expression level of a HSNA or HSP. In many cases, the use of another cancer marker will decrease the likelihood of false positives or false negatives. In one embodiment, the one or more other cancer markers include other HSNA or HSPs as disclosed herein. Other cancer markers useful in the present invention will depend on the cancer being tested and are known to those of skill in the art. In a preferred embodiment, at least one other cancer
15 marker in addition to a particular HSNA or HSP is measured. In a more preferred embodiment, at least two other additional cancer markers are used. In an even more preferred embodiment, at least three, more preferably at least five, even more preferably at least ten additional cancer markers are used.

20 *Diagnosing*

In one aspect, the invention provides a method for determining the expression levels and/or structural alterations of one or more HSNA and/or HSP in a sample from a patient suspected of having hepatic cancer. In general, the method comprises the steps of obtaining the sample from the patient, determining the expression level or structural
25 alterations of a HSNA and/or HSP and then ascertaining whether the patient has hepatic cancer from the expression level of the HSNA or HSP. In general, if high expression relative to a control of a HSNA or HSP is indicative of hepatic cancer, a diagnostic assay is considered positive if the level of expression of the HSNA or HSP is at least one and a half times higher, and more preferably are at least two times higher, still more preferably
30 five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of a HSNA or HSP is indicative of hepatic cancer, a diagnostic assay is considered positive if the level of expression of the HSNA or HSP is at

least one and a half times lower, and more preferably are at least two times lower, still more preferably five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control. The normal human control may be from a different patient or from uninvolved tissue of the same patient.

The present invention also provides a method of determining whether hepatic cancer has metastasized in a patient. One may identify whether the hepatic cancer has metastasized by measuring the expression levels and/or structural alterations of one or more HSNA and/or HSPs in a variety of tissues. The presence of a HSNA or HSP in a certain tissue at levels higher than that of corresponding noncancerous tissue (*e.g.*, the same tissue from another individual) is indicative of metastasis if high level expression of a HSNA or HSP is associated with hepatic cancer. Similarly, the presence of a HSNA or HSP in a tissue at levels lower than that of corresponding noncancerous tissue is indicative of metastasis if low level expression of a HSNA or HSP is associated with hepatic cancer. Further, the presence of a structurally altered HSNA or HSP that is associated with hepatic cancer is also indicative of metastasis.

In general, if high expression relative to a control of a HSNA or HSP is indicative of metastasis, an assay for metastasis is considered positive if the level of expression of the HSNA or HSP is at least one and a half times higher, and more preferably are at least two times higher, still more preferably five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of a HSNA or HSP is indicative of metastasis, an assay for metastasis is considered positive if the level of expression of the HSNA or HSP is at least one and a half times lower, and more preferably are at least two times lower, still more preferably five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control.

Staging

The invention also provides a method of staging hepatic cancer in a human patient. The method comprises identifying a human patient having hepatic cancer and analyzing cells, tissues or bodily fluids from such human patient for expression levels and/or structural alterations of one or more HSNA or HSPs. First, one or more tumors from a

variety of patients are staged according to procedures well known in the art, and the expression levels of one or more HSNA or HSPs is determined for each stage to obtain a standard expression level for each HSNA and HSP. Then, the HSNA or HSP expression levels of the HSNA or HSP are determined in a biological sample from a patient whose stage of cancer is not known. The HSNA or HSP expression levels from the patient are then compared to the standard expression level. By comparing the expression level of the HSNA and HSPs from the patient to the standard expression levels, one may determine the stage of the tumor. The same procedure may be followed using structural alterations of a HSNA or HSP to determine the stage of a hepatic cancer.

10 *Monitoring*

Further provided is a method of monitoring hepatic cancer in a human patient. One may monitor a human patient to determine whether there has been metastasis and, if there has been, when metastasis began to occur. One may also monitor a human patient to determine whether a preneoplastic lesion has become cancerous. One may also monitor a human patient to determine whether a therapy, *e.g.*, chemotherapy, radiotherapy or surgery, has decreased or eliminated the hepatic cancer. The monitoring may determine if there has been a reoccurrence and, if so, determine its nature. The method comprises identifying a human patient that one wants to monitor for hepatic cancer, periodically analyzing cells, tissues or bodily fluids from such human patient for expression levels of one or more HSNA or HSPs, and comparing the HSNA or HSP levels over time to those HSNA or HSP expression levels obtained previously. Patients may also be monitored by measuring one or more structural alterations in a HSNA or HSP that are associated with hepatic cancer.

If increased expression of a HSNA or HSP is associated with metastasis, treatment failure, or conversion of a preneoplastic lesion to a cancerous lesion, then detecting an increase in the expression level of a HSNA or HSP indicates that the tumor is metastasizing, that treatment has failed or that the lesion is cancerous, respectively. One having ordinary skill in the art would recognize that if this were the case, then a decreased expression level would be indicative of no metastasis, effective therapy or failure to progress to a neoplastic lesion. If decreased expression of a HSNA or HSP is associated with metastasis, treatment failure, or conversion of a preneoplastic lesion to a cancerous lesion, then detecting a decrease in the expression level of a HSNA or HSP indicates that

the tumor is metastasizing, that treatment has failed or that the lesion is cancerous, respectively. In a preferred embodiment, the levels of HSNAs or HSPs are determined from the same cell type, tissue or bodily fluid as prior patient samples. Monitoring a patient for onset of hepatic cancer metastasis is periodic and preferably is done on a quarterly basis, but may be done more or less frequently.

The methods described herein can further be utilized as prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with increased or decreased expression levels of a HSNA and/or HSP. The present invention provides a method in which a test sample is obtained from a human patient and one or more HSNAs and/or HSPs are detected. The presence of higher (or lower) HSNA or HSP levels as compared to normal human controls is diagnostic for the human patient being at risk for developing cancer, particularly hepatic cancer. The effectiveness of therapeutic agents to decrease (or increase) expression or activity of one or more HSNAs and/or HSPs of the invention can also be monitored by analyzing levels of expression of the HSNAs and/or HSPs in a human patient in clinical trials or in *in vitro* screening assays such as in human cells. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the human patient or cells, as the case may be, to the agent being tested.

Detection of Genetic Lesions or Mutations

The methods of the present invention can also be used to detect genetic lesions or mutations in a HSG, thereby determining if a human with the genetic lesion is susceptible to developing hepatic cancer or to determine what genetic lesions are responsible, or are partly responsible, for a person's existing hepatic cancer. Genetic lesions can be detected, for example, by ascertaining the existence of a deletion, insertion and/or substitution of one or more nucleotides from the HSGs of this invention, a chromosomal rearrangement of a HSG, an aberrant modification of a HSG (such as of the methylation pattern of the genomic DNA), or allelic loss of a HSG. Methods to detect such lesions in the HSG of this invention are known to those having ordinary skill in the art following the teachings of the specification.

Methods of Detecting Noncancerous hepatic Diseases

The present invention also provides methods for determining the expression levels and/or structural alterations of one or more HSNAs and/or HSPs in a sample from a

patient suspected of having or known to have a noncancerous hepatic disease. In general, the method comprises the steps of obtaining a sample from the patient, determining the expression level or structural alterations of a HSNA and/or HSP, comparing the expression level or structural alteration of the HSNA or HSP to a normal hepatic control, and then ascertaining whether the patient has a noncancerous hepatic disease. In general, if high expression relative to a control of a HSNA or HSP is indicative of a particular noncancerous hepatic disease, a diagnostic assay is considered positive if the level of expression of the HSNA or HSP is at least two times higher, and more preferably are at least five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of a HSNA or HSP is indicative of a noncancerous hepatic disease, a diagnostic assay is considered positive if the level of expression of the HSNA or HSP is at least two times lower, more preferably are at least five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control. The normal human control may be from a different patient or from uninvolved tissue of the same patient.

One having ordinary skill in the art may determine whether a HSNA and/or HSP is associated with a particular noncancerous hepatic disease by obtaining hepatic tissue from a patient having a noncancerous hepatic disease of interest and determining which HSNAs and/or HSPs are expressed in the tissue at either a higher or a lower level than in normal hepatic tissue. In another embodiment, one may determine whether a HSNA or HSP exhibits structural alterations in a particular noncancerous hepatic disease state by obtaining hepatic tissue from a patient having a noncancerous hepatic disease of interest and determining the structural alterations in one or more HSNAs and/or HSPs relative to normal hepatic tissue.

Methods for Identifying hepatic Tissue

In another aspect, the invention provides methods for identifying hepatic tissue. These methods are particularly useful in, *e.g.*, forensic science, hepatic cell differentiation and development, and in tissue engineering.

In one embodiment, the invention provides a method for determining whether a sample is hepatic tissue or has hepatic tissue-like characteristics. The method comprises the steps of providing a sample suspected of comprising hepatic tissue or having hepatic

tissue-like characteristics, determining whether the sample expresses one or more HSNAs and/or HSPs, and, if the sample expresses one or more HSNAs and/or HSPs, concluding that the sample comprises hepatic tissue. In a preferred embodiment, the HSNA encodes a polypeptide having an amino acid sequence selected from SEQ ID NO: 410-611, or a
5 homolog, allelic variant or fragment thereof. In a more preferred embodiment, the HSNA has a nucleotide sequence selected from SEQ ID NO: 1-409, or a hybridizing nucleic acid, an allelic variant or a part thereof. Determining whether a sample expresses a HSNA can be accomplished by any method known in the art. Preferred methods include hybridization to microarrays, Northern blot hybridization, and quantitative or qualitative
10 RT-PCR. In another preferred embodiment, the method can be practiced by determining whether a HSP is expressed. Determining whether a sample expresses a HSP can be accomplished by any method known in the art. Preferred methods include Western blot, ELISA, RIA and 2D PAGE. In one embodiment, the HSP has an amino acid sequence selected from SEQ ID NO: 410-611, or a homolog, allelic variant or fragment thereof. In
15 another preferred embodiment, the expression of at least two HSNAs and/or HSPs is determined. In a more preferred embodiment, the expression of at least three, more preferably four and even more preferably five HSNAs and/or HSPs are determined.

In one embodiment, the method can be used to determine whether an unknown tissue is hepatic tissue. This is particularly useful in forensic science, in which small,
20 damaged pieces of tissues that are not identifiable by microscopic or other means are recovered from a crime or accident scene. In another embodiment, the method can be used to determine whether a tissue is differentiating or developing into hepatic tissue. This is important in monitoring the effects of the addition of various agents to cell or tissue culture, *e.g.*, in producing new hepatic tissue by tissue engineering. These agents
25 include, *e.g.*, growth and differentiation factors, extracellular matrix proteins and culture medium. Other factors that may be measured for effects on tissue development and differentiation include gene transfer into the cells or tissues, alterations in pH, aqueous:air interface and various other culture conditions.

Methods for Producing and Modifying hepatic Tissue

30 In another aspect, the invention provides methods for producing engineered hepatic tissue or cells. In one embodiment, the method comprises the steps of providing cells, introducing a HSNA or a HSG into the cells, and growing the cells under conditions

in which they exhibit one or more properties of hepatic tissue cells. In a preferred embodiment, the cells are pluripotent. As is well known in the art, normal hepatic tissue comprises a large number of different cell types. Thus, in one embodiment, the engineered hepatic tissue or cells comprises one of these cell types. In another embodiment, the engineered hepatic tissue or cells comprises more than one hepatic cell type. Further, the culture conditions of the cells or tissue may require manipulation in order to achieve full differentiation and development of the hepatic cell tissue. Methods for manipulating culture conditions are well known in the art.

Nucleic acid molecules encoding one or more HSPs are introduced into cells, preferably pluripotent cells. In a preferred embodiment, the nucleic acid molecules encode HSPs having amino acid sequences selected from SEQ ID NO: 410-611, or homologous proteins, analogs, allelic variants or fragments thereof. In a more preferred embodiment, the nucleic acid molecules have a nucleotide sequence selected from SEQ ID NO: 1-409, or hybridizing nucleic acids, allelic variants or parts thereof. In another highly preferred embodiment, a HSG is introduced into the cells. Expression vectors and methods of introducing nucleic acid molecules into cells are well known in the art and are described in detail, *supra*.

Artificial hepatic tissue may be used to treat patients who have lost some or all of their hepatic function.

Pharmaceutical Compositions

In another aspect, the invention provides pharmaceutical compositions comprising the nucleic acid molecules, polypeptides, fusion proteins, antibodies, antibody derivatives, antibody fragments, agonists, antagonists, or inhibitors of the present invention. In a preferred embodiment, the pharmaceutical composition comprises a HSNA or part thereof. In a more preferred embodiment, the HSNA has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-409, a nucleic acid that hybridizes thereto, an allelic variant thereof, or a nucleic acid that has substantial sequence identity thereto. In another preferred embodiment, the pharmaceutical composition comprises a HSP or fragment thereof. In a more preferred embodiment, the pharmaceutical composition comprises a HSP having an amino acid sequence that is selected from the group consisting of SEQ ID NO: 410-611, a polypeptide that is homologous thereto, a fusion protein comprising all or a portion of the polypeptide, or an analog or derivative thereof. In another preferred

embodiment, the pharmaceutical composition comprises an anti-HSP antibody, preferably an antibody that specifically binds to a HSP having an amino acid that is selected from the group consisting of SEQ ID NO: 410-611, or an antibody that binds to a polypeptide that is homologous thereto, a fusion protein comprising all or a portion of the polypeptide, or
5 an analog or derivative thereof.

Such a composition typically contains from about 0.1 to 90% by weight of a therapeutic agent of the invention formulated in and/or with a pharmaceutically acceptable carrier or excipient.

Pharmaceutical formulation is a well-established art that is further described in
10 Gennaro (ed.), Remington: The Science and Practice of Pharmacy, 20th ed., Lippincott, Williams & Wilkins (2000); Ansel *et al.*, Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th ed., Lippincott Williams & Wilkins (1999); and Kibbe (ed.), Handbook of Pharmaceutical Excipients American Pharmaceutical Association, 3rd ed. (2000) and thus need not be described in detail herein.

15 Briefly, formulation of the pharmaceutical compositions of the present invention will depend upon the route chosen for administration. The pharmaceutical compositions utilized in this invention can be administered by various routes including both enteral and parenteral routes, including oral, intravenous, intramuscular, subcutaneous, inhalation, topical, sublingual, rectal, intra-arterial, intramedullary, intrathecal, intraventricular,
20 transmucosal, transdermal, intranasal, intraperitoneal, intrapulmonary, and intrauterine.

Oral dosage forms can be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Solid formulations of the compositions for oral administration can contain suitable carriers or excipients, such as carbohydrate or protein fillers, such as sugars, including
25 lactose, sucrose, mannitol, or sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, or microcrystalline cellulose; gums including arabic and tragacanth; proteins such as gelatin and collagen; inorganics, such as kaolin, calcium carbonate, dicalcium phosphate, sodium chloride; and other agents such as acacia and
30 alginic acid.

Agents that facilitate disintegration and/or solubilization can be added, such as the cross-linked polyvinyl pyrrolidone, agar, alginic acid, or a salt thereof, such as sodium alginate, microcrystalline cellulose, cornstarch, sodium starch glycolate, and alginic acid.

Tablet binders that can be used include acacia, methylcellulose, sodium carboxymethylcellulose, polyvinylpyrrolidone (Povidone™), hydroxypropyl methylcellulose, sucrose, starch and ethylcellulose.

Lubricants that can be used include magnesium stearates, stearic acid, silicone
5 fluid, talc, waxes, oils, and colloidal silica.

Fillers, agents that facilitate disintegration and/or solubilization, tablet binders and lubricants, including the aforementioned, can be used singly or in combination.

Solid oral dosage forms need not be uniform throughout. For example, dragee
10 cores can be used in conjunction with suitable coatings, such as concentrated sugar solutions, which can also contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures.

Oral dosage forms of the present invention include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or
15 sorbitol. Push-fit capsules can contain active ingredients mixed with a filler or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with or without stabilizers.

20 Additionally, dyestuffs or pigments can be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, *i.e.*, dosage.

Liquid formulations of the pharmaceutical compositions for oral (enteral) administration are prepared in water or other aqueous vehicles and can contain various suspending agents such as methylcellulose, alginates, tragacanth, pectin, kelgin,
25 carrageenan, acacia, polyvinylpyrrolidone, and polyvinyl alcohol. The liquid formulations can also include solutions, emulsions, syrups and elixirs containing, together with the active compound(s), wetting agents, sweeteners, and coloring and flavoring agents.

The pharmaceutical compositions of the present invention can also be formulated for parenteral administration. Formulations for parenteral administration can be in the
30 form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions.

For intravenous injection, water soluble versions of the compounds of the present invention are formulated in, or if provided as a lyophilate, mixed with, a physiologically acceptable fluid vehicle, such as 5% dextrose ("D5"), physiologically buffered saline,

0.9% saline, Hanks' solution, or Ringer's solution. Intravenous formulations may include carriers, excipients or stabilizers including, without limitation, calcium, human serum albumin, citrate, acetate, calcium chloride, carbonate, and other salts.

Intramuscular preparations, *e.g.* a sterile formulation of a suitable soluble salt form
5 of the compounds of the present invention, can be dissolved and administered in a pharmaceutical excipient such as Water-for-Injection, 0.9% saline, or 5% glucose solution. Alternatively, a suitable insoluble form of the compound can be prepared and administered as a suspension in an aqueous base or a pharmaceutically acceptable oil base, such as an ester of a long chain fatty acid (*e.g.*, ethyl oleate), fatty oils such as sesame oil,
10 triglycerides, or liposomes.

Parenteral formulations of the compositions can contain various carriers such as vegetable oils, dimethylacetamide, dimethylformamide, ethyl lactate, ethyl carbonate, isopropyl myristate, ethanol, polyols (glycerol, propylene glycol, liquid polyethylene glycol, and the like).

15 Aqueous injection suspensions can also contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Non-lipid polycationic amino polymers can also be used for delivery. Optionally, the suspension can also contain suitable stabilizers or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

20 Pharmaceutical compositions of the present invention can also be formulated to permit injectable, long-term, deposition. Injectable depot forms may be made by forming microencapsulated matrices of the compound in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of
25 other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in microemulsions that are compatible with body tissues.

The pharmaceutical compositions of the present invention can be administered topically. For topical use the compounds of the present invention can also be prepared in
30 suitable forms to be applied to the skin, or mucus membranes of the nose and throat, and can take the form of lotions, creams, ointments, liquid sprays or inhalants, drops, tinctures, lozenges, or throat paints. Such topical formulations further can include chemical compounds such as dimethylsulfoxide (DMSO) to facilitate surface penetration of the

active ingredient. In other transdermal formulations, typically in patch-delivered formulations, the pharmaceutically active compound is formulated with one or more skin penetrants, such as 2-N-methyl-pyrrolidone (NMP) or Azone. A topical semi-solid ointment formulation typically contains a concentration of the active ingredient from
5 about 1 to 20%, *e.g.*, 5 to 10%, in a carrier such as a pharmaceutical cream base.

For application to the eyes or ears, the compounds of the present invention can be presented in liquid or semi-liquid form formulated in hydrophobic or hydrophilic bases as ointments, creams, lotions, paints or powders.

For rectal administration the compounds of the present invention can be
10 administered in the form of suppositories admixed with conventional carriers such as cocoa butter, wax or other glyceride.

Inhalation formulations can also readily be formulated. For inhalation, various powder and liquid formulations can be prepared. For aerosol preparations, a sterile formulation of the compound or salt form of the compound may be used in inhalers, such
15 as metered dose inhalers, and nebulizers. Aerosolized forms may be especially useful for treating respiratory disorders.

Alternatively, the compounds of the present invention can be in powder form for reconstitution in the appropriate pharmaceutically acceptable carrier at the time of delivery.

20 The pharmaceutically active compound in the pharmaceutical compositions of the present invention can be provided as the salt of a variety of acids, including but not limited to hydrochloric, sulfuric, acetic, lactic, tartaric, malic, and succinic acid. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms.

25 After pharmaceutical compositions have been prepared, they are packaged in an appropriate container and labeled for treatment of an indicated condition.

The active compound will be present in an amount effective to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

30 A "therapeutically effective dose" refers to that amount of active ingredient, for example HSP polypeptide, fusion protein, or fragments thereof, antibodies specific for HSP, agonists, antagonists or inhibitors of HSP, which ameliorates the signs or symptoms

of the disease or prevent progression thereof; as would be understood in the medical arts, cure, although desired, is not required.

The therapeutically effective dose of the pharmaceutical agents of the present invention can be estimated initially by *in vitro* tests, such as cell culture assays, followed
5 by assay in model animals, usually mice, rats, rabbits, dogs, or pigs. The animal model can also be used to determine an initial preferred concentration range and route of administration.

For example, the ED50 (the dose therapeutically effective in 50% of the population) and LD50 (the dose lethal to 50% of the population) can be determined in one
10 or more cell culture of animal model systems. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as LD50/ED50. Pharmaceutical compositions that exhibit large therapeutic indices are preferred.

The data obtained from cell culture assays and animal studies are used in formulating an initial dosage range for human use, and preferably provide a range of
15 circulating concentrations that includes the ED50 with little or no toxicity. After administration, or between successive administrations, the circulating concentration of active agent varies within this range depending upon pharmacokinetic factors well known in the art, such as the dosage form employed, sensitivity of the patient, and the route of administration.

20 The exact dosage will be determined by the practitioner, in light of factors specific to the subject requiring treatment. Factors that can be taken into account by the practitioner include the severity of the disease state, general health of the subject, age, weight, gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long-acting
25 pharmaceutical compositions can be administered every 3 to 4 days, every week, or once every two weeks depending on half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from 0.1 to 100,000 micrograms, up to a total dose of about 1 g, depending upon the route of administration. Where the therapeutic agent is a protein or antibody of the present invention, the therapeutic protein or antibody
30 agent typically is administered at a daily dosage of 0.01 mg to 30 mg/kg of body weight of the patient (*e.g.*, 1mg/kg to 5 mg/kg). The pharmaceutical formulation can be administered in multiple doses per day, if desired, to achieve the total desired daily dose.

Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

Conventional methods, known to those of ordinary skill in the art of medicine, can be used to administer the pharmaceutical formulation(s) of the present invention to the patient. The pharmaceutical compositions of the present invention can be administered alone, or in combination with other therapeutic agents or interventions.

10 Therapeutic Methods

The present invention further provides methods of treating subjects having defects in a gene of the invention, *e.g.*, in expression, activity, distribution, localization, and/or solubility, which can manifest as a disorder of hepatic function. As used herein, "treating" includes all medically-acceptable types of therapeutic intervention, including palliation and prophylaxis (prevention) of disease. The term "treating" encompasses any improvement of a disease, including minor improvements. These methods are discussed below.

Gene Therapy and Vaccines

The isolated nucleic acids of the present invention can also be used to drive *in vivo* expression of the polypeptides of the present invention. *In vivo* expression can be driven from a vector, typically a viral vector, often a vector based upon a replication incompetent retrovirus, an adenovirus, or an adeno-associated virus (AAV), for the purpose of gene therapy. *In vivo* expression can also be driven from signals endogenous to the nucleic acid or from a vector, often a plasmid vector, such as pVAX1 (Invitrogen, Carlsbad, CA, USA), for purpose of "naked" nucleic acid vaccination, as further described in U.S. Patent Nos. 5,589,466; 5,679,647; 5,804,566; 5,830,877; 5,843,913; 5,880,104; 5,958,891; 5,985,847; 6,017,897; 6,110,898; 6,204,250, the disclosures of which are incorporated herein by reference in their entireties. For cancer therapy, it is preferred that the vector also be tumor-selective. *See, e.g.*, Doronin *et al.*, *J. Virol.* 75: 3314-24 (2001).

In another embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising a nucleic acid molecule of the present invention is administered. The nucleic acid molecule can be

delivered in a vector that drives expression of a HSP, fusion protein, or fragment thereof, or without such vector. Nucleic acid compositions that can drive expression of a HSP are administered, for example, to complement a deficiency in the native HSP, or as DNA vaccines. Expression vectors derived from virus, replication deficient retroviruses,
5 adenovirus, adeno-associated (AAV) virus, herpes virus, or vaccinia virus can be used as can plasmids. *See, e.g., Cid-Arregui, supra.* In a preferred embodiment, the nucleic acid molecule encodes a HSP having the amino acid sequence of SEQ ID NO: 410-611, or a fragment, fusion protein, allelic variant or homolog thereof.

In still other therapeutic methods of the present invention, pharmaceutical
10 compositions comprising host cells that express a HSP, fusions, or fragments thereof can be administered. In such cases, the cells are typically autologous, so as to circumvent xenogeneic or allotypic rejection, and are administered to complement defects in HSP production or activity. In a preferred embodiment, the nucleic acid molecules in the cells encode a HSP having the amino acid sequence of SEQ ID NO: 410-611, or a fragment,
15 fusion protein, allelic variant or homolog thereof.

Antisense Administration

Antisense nucleic acid compositions, or vectors that drive expression of a HSG antisense nucleic acid, are administered to downregulate transcription and/or translation of a HSG in circumstances in which excessive production, or production of aberrant protein,
20 is the pathophysiologic basis of disease.

Antisense compositions useful in therapy can have a sequence that is complementary to coding or to noncoding regions of a HSG. For example, oligonucleotides derived from the transcription initiation site, *e.g.,* between positions -10 and +10 from the start site, are preferred.

25 Catalytic antisense compositions, such as ribozymes, that are capable of sequence-specific hybridization to HSG transcripts, are also useful in therapy. *See, e.g., Phylactou, Adv. Drug Deliv. Rev. 44(2-3): 97-108 (2000); Phylactou et al., Hum. Mol. Genet. 7(10): 1649-53 (1998); Rossi, Ciba Found. Symp. 209: 195-204 (1997); and Sigurdsson et al., Trends Biotechnol. 13(8): 286-9 (1995).*

30 Other nucleic acids useful in the therapeutic methods of the present invention are those that are capable of triplex helix formation in or near the HSG genomic locus. Such triplexing oligonucleotides are able to inhibit transcription. *See, e.g., Intody et al., Nucleic*

Acids Res. 28(21): 4283-90 (2000); and McGuffie *et al.*, *Cancer Res.* 60(14): 3790-9 (2000). Pharmaceutical compositions comprising such triplex forming oligos (TFOs) are administered in circumstances in which excessive production, or production of aberrant protein, is a pathophysiologic basis of disease.

5 In a preferred embodiment, the antisense molecule is derived from a nucleic acid molecule encoding a HSP, preferably a HSP comprising an amino acid sequence of SEQ ID NO: 410-611, or a fragment, allelic variant or homolog thereof. In a more preferred embodiment, the antisense molecule is derived from a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-409, or a part, allelic variant, substantially similar
10 or hybridizing nucleic acid thereof.

Polypeptide Administration

In one embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising a HSP, a fusion protein, fragment, analog or derivative thereof is administered to a subject with a
15 clinically-significant HSP defect.

Protein compositions are administered, for example, to complement a deficiency in native HSP. In other embodiments, protein compositions are administered as a vaccine to elicit a humoral and/or cellular immune response to HSP. The immune response can be used to modulate activity of HSP or, depending on the immunogen, to immunize against
20 aberrant or aberrantly expressed forms, such as mutant or inappropriately expressed isoforms. In yet other embodiments, protein fusions having a toxic moiety are administered to ablate cells that aberrantly accumulate HSP.

In a preferred embodiment, the polypeptide administered is a HSP comprising an amino acid sequence of SEQ ID NO: 410-611, or a fusion protein, allelic variant,
25 homolog, analog or derivative thereof. In a more preferred embodiment, the polypeptide is encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-409, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Antibody, Agonist and Antagonist Administration

In another embodiment of the therapeutic methods of the present invention, a
30 therapeutically effective amount of a pharmaceutical composition comprising an antibody (including fragment or derivative thereof) of the present invention is administered. As is well known, antibody compositions are administered, for example, to antagonize activity

of HSP, or to target therapeutic agents to sites of HSP presence and/or accumulation. In a preferred embodiment, the antibody specifically binds to a HSP comprising an amino acid sequence of SEQ ID NO: 410-611, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the antibody specifically binds to a HSP encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-409, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

The present invention also provides methods for identifying modulators which bind to a HSP or have a modulatory effect on the expression or activity of a HSP. Modulators which decrease the expression or activity of HSP (antagonists) are believed to be useful in treating hepatic cancer. Such screening assays are known to those of skill in the art and include, without limitation, cell-based assays and cell-free assays. Small molecules predicted via computer imaging to specifically bind to regions of a HSP can also be designed, synthesized and tested for use in the imaging and treatment of hepatic cancer. Further, libraries of molecules can be screened for potential anticancer agents by assessing the ability of the molecule to bind to the HSPs identified herein. Molecules identified in the library as being capable of binding to a HSP are key candidates for further evaluation for use in the treatment of hepatic cancer. In a preferred embodiment, these molecules will downregulate expression and/or activity of a HSP in cells.

In another embodiment of the therapeutic methods of the present invention, a pharmaceutical composition comprising a non-antibody antagonist of HSP is administered. Antagonists of HSP can be produced using methods generally known in the art. In particular, purified HSP can be used to screen libraries of pharmaceutical agents, often combinatorial libraries of small molecules, to identify those that specifically bind and antagonize at least one activity of a HSP.

In other embodiments a pharmaceutical composition comprising an agonist of a HSP is administered. Agonists can be identified using methods analogous to those used to identify antagonists.

In a preferred embodiment, the antagonist or agonist specifically binds to and antagonizes or agonizes, respectively, a HSP comprising an amino acid sequence of SEQ ID NO: 410-611, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the antagonist or agonist specifically binds to and antagonizes or agonizes, respectively, a HSP encoded by a nucleic acid molecule having a

nucleotide sequence of SEQ ID NO: 1-409, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Targeting hepatic Tissue

5 The invention also provides a method in which a polypeptide of the invention, or an antibody thereto, is linked to a therapeutic agent such that it can be delivered to the hepatic or to specific cells in the hepatic. In a preferred embodiment, an anti-HSP antibody is linked to a therapeutic agent and is administered to a patient in need of such therapeutic agent. The therapeutic agent may be a toxin, if hepatic tissue needs to be
10 selectively destroyed. This would be useful for targeting and killing hepatic cancer cells. In another embodiment, the therapeutic agent may be a growth or differentiation factor, which would be useful for promoting hepatic cell function.

 In another embodiment, an anti-HSP antibody may be linked to an imaging agent that can be detected using, *e.g.*, magnetic resonance imaging, CT or PET. This would be
15 useful for determining and monitoring hepatic function, identifying hepatic cancer tumors, and identifying noncancerous hepatic diseases.

EXAMPLES

Example 1: Gene Expression analysis

Custom CLASP Experiment

20 HSGs were identified by a systematic analysis of gene expression data in the LIFESEQ® Gold database available from Incyte Genomics Inc (Palo Alto, CA) using the data mining software package CLASP™ (Candidate Lead Automatic Search Program). CLASP™ is a set of algorithms that interrogate Incyte's database to identify genes that are both specific to particular tissue types as well as differentially expressed in tissues from
25 patients with cancer. LifeSeq® Gold contains information about which genes are expressed in various tissues in the body and about the dynamics of expression in both normal and diseased states. CLASP™ first sorts the LifeSeq® Gold database into defined tissue types, such as breast, ovary and prostate. CLASP™ categorizes each tissue sample by disease state. Disease states include "healthy," "cancer," "associated with cancer,"
30 "other disease" and "other." Categorizing the disease states improves our ability to identify tissue and cancer-specific molecular targets. CLASP™ then performs a

simultaneous parallel search for genes that are expressed both (1) selectively in the defined tissue type compared to other tissue types and (2) differentially in the "cancer" disease state compared to the other disease states affecting the same, or different, tissues. This sorting is accomplished by using mathematical and statistical filters that specify the minimum change in expression levels and the minimum frequency that the differential expression pattern must be observed across the tissue samples for the gene to be considered statistically significant. The CLASP™ algorithm quantifies the relative abundance of a particular gene in each tissue type and in each disease state.

To find the HSGs of this invention, the following specific CLASP™ profiles were utilized: tissue-specific expression (CLASP 1), detectable expression only in cancer tissue (CLASP 2), maximal expression in cancer (CLASP 4) and differential expression in cancer tissue (CLASP 5). cDNA libraries were divided into 60 unique tissue types (early versions of LifeSeq® had 48 tissue types). Genes or ESTs were grouped into "gene bins," where each bin is a cluster of sequences grouped together where they share a common contig. The expression level for each gene bin was calculated for each tissue type. Differential expression significance was calculated with rigorous statistical significant testing taking into account variations in sample size and relative gene abundance in different libraries and within each library (for the equations used to determine statistically significant expression see Audic and Claverie "The significance of digital gene expression profiles," Genome Res 7(10): 986-995 (1997), including Equation 1 on page 987 and Equation 2 on page 988, the contents of which are incorporated by reference). Differentially expressed tissue-specific genes were selected based on the percentage abundance level in the targeted tissue versus all the other tissues (tissue-specificity). The expression levels for each gene in libraries of normal tissues or non-tumor tissues from cancer patients were compared with the expression levels in tissue libraries associated with tumor or disease (cancer-specificity). The results were analyzed for statistical significance.

The selection of the target genes meeting the rigorous CLASP™ profile criteria were as follows:

- (a) CLASP 1: tissue-specific expression: To qualify as a CLASP 1 candidate, a gene must exhibit statistically significant expression in the tissue of interest compared to all other tissues. Only if the gene exhibits such differential

expression with a 90% of confidence level is it selected as a CLASP 1 candidate.

- (b) CLASP 2: detectable expression only in cancer tissue: To qualify as a CLASP 2 candidate, a gene must exhibit detectable expression in tumor tissues and undetectable expression in libraries from normal individuals and libraries from normal tissue obtained from diseased patients. In addition, such a gene must also exhibit further specificity for the tumor tissues of interest.
- (c) CLASP 4: maximum differential expression in cancer: To qualify as a CLASP 4 candidate, the lead must exhibit be one of the top50 genes showing maximal differential expression in cancer tissues. In addition, such a gene must also exhibit further specificity for the tumor tissues of interest.
- (d) CLASP 5: differential expression in cancer tissue: To qualify as a CLASP 5 candidate, a gene must be differentially expressed in tumor libraries in the tissue of interest compared to normal libraries for all tissues. Only if the gene exhibits such differential expression with a 90% of confidence level is it selected as a CLASP 5 candidate.

The CLASP scores for SEQ ID NO: 1-409 are listed below:

Expression data is not presented for many specific splice variants, however at least one transcript for the splice variant family is supported by expression data shown in the table.

- Splice variants may share similar regions among various transcripts and therefore data for one variant may be relevant to another. This supporting data is available on request.

There are 2 values for each organ in the format 9 - 0.9999. The first represent the number of occurrences of the gene in the given organ. The 2nd number represents the percentage of the expression of the gene in the given organ.

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|--------------------|--------------------|------------------|--------------|--------------|--------------|--|--|
| DEX0374_1. nt.1 | SEQID NO. 1 | CLASP2 | LIV .0048 | | | | |
| DEX0374_2. nt.1 | SEQID NO. 3 | CLASP2 | LIV .0081 | | | | |
| DEX0374_3. nt.1 | SEQID NO. 5 | CLASP5 CLASP1 | LIV .0057 | BRN .0001 | INS .0019 | | |
| DEX0374_4. nt.1 | SEQID NO. 30 | CLASP2 | LIV .0081 | | | | |
| DEX0374_5. nt.1 | SEQID NO. 32 | CLASP2 | LIV .0048 | | | | |
| DEX0374_6. nt.1 | SEQID NO. 34 | CLASP2 | LIV .0081 | | | | |
| DEX0374_7. | SEQID | CLASP1 | LIV | SKN | STO | | |

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|---------------------|---------------------|------------------|--------------|--------------|-------|--|--|
| nt.1 | NO. 51 | | .0032 | .0015 | .0021 | | |
| DEX0374_8. nt.1 | SEQID NO. 53 | CLASP2 | LIV .0081 | | | | |
| DEX0374_8. nt.2 | SEQID NO. 54 | CLASP2 | LIV .0081 | | | | |
| DEX0374_9. nt.1 | SEQID NO. 56 | CLASP2 CLASP1 | LIV .0194 | BRN .0001 | | | |
| DEX0374_10 .nt.1 | SEQID NO. 58 | CLASP2 CLASP1 | LIV .0194 | | | | |
| DEX0374_11 .nt.1 | SEQID NO. 60 | CLASP2 | LIV .0081 | | | | |
| DEX0374_12 .nt.1 | SEQID NO. 65 | CLASP2 | LIV .0137 | | | | |
| DEX0374_13 .nt.1 | SEQID NO. 67 | CLASP2 | LIV .0048 | | | | |
| DEX0374_14 .nt.1 | SEQID NO. 69 | CLASP2 | LIV .0129 | | | | |
| DEX0374_15 .nt.1 | SEQID NO. 70 | CLASP2 | LIV .0048 | | | | |
| DEX0374_15 .nt.2 | SEQID NO. 71 | CLASP2 | LIV .0048 | | | | |
| DEX0374_16 .nt.1 | SEQID NO. 73 | CLASP1 | LIV .0032 | | | | |
| DEX0374_16 .nt.2 | SEQID NO. 74 | CLASP1 | LIV .0032 | | | | |
| DEX0374_17 .nt.1 | SEQID NO. 104 | CLASP2 | LIV .0081 | | | | |
| DEX0374_18 .nt.1 | SEQID NO. 113 | CLASP2 | LIV .0081 | | | | |
| DEX0374_18 .nt.2 | SEQID NO. 114 | CLASP2 | LIV .0081 | | | | |
| DEX0374_19 .nt.1 | SEQID NO. 117 | CLASP2 | LIV .0081 | | | | |
| DEX0374_20 .nt.1 | SEQID NO. 119 | CLASP2 | LIV .0137 | | | | |
| DEX0374_20 .nt.2 | SEQID NO. 120 | CLASP2 | LIV .0137 | | | | |
| DEX0374_21 .nt.1 | SEQID NO. 121 | CLASP2 | LIV .0081 | | | | |

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|---------------------|---------------------|------------------|--------------|--------------|--------------|--------------|--------------|
| DEX0374_22 .nt.1 | SEQID NO. 123 | CLASP2 | LIV .0048 | LNG .0011 | | | |
| DEX0374_22 .nt.2 | SEQID NO. 124 | CLASP2 | LIV .0048 | LNG .0011 | | | |
| DEX0374_23 .nt.1 | SEQID NO. 126 | CLASP2 | LIV .0048 | | | | |
| DEX0374_23 .nt.2 | SEQID NO. 127 | CLASP2 | LIV .0048 | | | | |
| DEX0374_24 .nt.1 | SEQID NO. 131 | CLASP2 | LIV .0081 | | | | |
| DEX0374_25 .nt.1 | SEQID NO. 134 | CLASP2 | LIV .0129 | | | | |
| DEX0374_26 .nt.1 | SEQID NO. 136 | CLASP2 CLASP1 | LIV .0072 | FTS .0004 | UNC .0011 | | |
| DEX0374_27 .nt.1 | SEQID NO. 137 | CLASP5 CLASP1 | LIV .0057 | LMN .0017 | | | |
| DEX0374_28 .nt.1 | SEQID NO. 139 | CLASP1 | LIV .0043 | UNC .0011 | | | |
| DEX0374_28 .nt.2 | SEQID NO. 140 | CLASP1 | LIV .0043 | UNC .0011 | | | |
| DEX0374_29 .nt.1 | SEQID NO. 142 | CLASP2 | LIV .0048 | | | | |
| DEX0374_29 .nt.2 | SEQID NO. 143 | CLASP2 | LIV .0048 | | | | |
| DEX0374_30 .nt.1 | SEQID NO. 145 | CLASP5 CLASP1 | LIV .0057 | BLO .0003 | PRO .0003 | FTS .0004 | INL .0004 |
| DEX0374_31 .nt.1 | SEQID NO. 147 | CLASP2 | LIV .0081 | | | | |
| DEX0374_31 .nt.2 | SEQID NO. 148 | CLASP2 | LIV .0081 | | | | |
| DEX0374_32 .nt.1 | SEQID NO. 150 | CLASP2 | LIV .0048 | | | | |
| DEX0374_33 .nt.1 | SEQID NO. 152 | CLASP5 CLASP1 | LIV .0057 | MAM .0008 | | | |
| DEX0374_34 .nt.1 | SEQID NO. 154 | CLASP2 | LIV .0048 | | | | |
| DEX0374_35 .nt.1 | SEQID NO. 157 | CLASP2 | LIV .0081 | | | | |
| DEX0374_36 .nt.1 | SEQID NO. | CLASP1 | LIV .0032 | | | | |

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|---------------------|---------------------|------------------|--------------|--------------|--------------|--|--|
| | 159 | | | | | | |
| DEX0374_37 .nt.1 | SEQID NO. 162 | CLASP2 | LIV .0048 | | | | |
| DEX0374_38 .nt.1 | SEQID NO. 164 | CLASP2 | LIV .0081 | INL .0027 | | | |
| DEX0374_38 .nt.2 | SEQID NO. 165 | CLASP2 | LIV .0081 | INL .0027 | | | |
| DEX0374_39 .nt.1 | SEQID NO. 167 | CLASP1 | LIV .0065 | | | | |
| DEX0374_39 .nt.2 | SEQID NO. 168 | CLASP1 | LIV .0065 | | | | |
| DEX0374_40 .nt.1 | SEQID NO. 170 | CLASP2 | LIV .0081 | | | | |
| DEX0374_41 .nt.1 | SEQID NO. 172 | CLASP2 CLASP1 | LIV .0072 | FTS .0004 | UNC .0011 | | |
| DEX0374_42 .nt.1 | SEQID NO. 174 | CLASP2 | LIV .0048 | | | | |
| DEX0374_43 .nt.1 | SEQID NO. 176 | CLASP2 | LIV .0081 | | | | |
| DEX0374_43 .nt.2 | SEQID NO. 177 | CLASP2 | LIV .0081 | | | | |
| DEX0374_44 .nt.1 | SEQID NO. 180 | CLASP1 | LIV .0032 | | | | |
| DEX0374_45 .nt.1 | SEQID NO. 182 | CLASP2 | LIV .0081 | | | | |
| DEX0374_46 .nt.1 | SEQID NO. 184 | CLASP2 | LIV .0081 | BRN .0021 | | | |
| DEX0374_47 .nt.1 | SEQID NO. 186 | CLASP2 CLASP1 | LIV .0122 | THR .002 | BMR .0029 | | |
| DEX0374_47 .nt.2 | SEQID NO. 187 | CLASP2 CLASP1 | LIV .0122 | THR .002 | BMR .0029 | | |
| DEX0374_47 .nt.3 | SEQID NO. 188 | CLASP2 CLASP1 | LIV .0122 | THR .002 | BMR .0029 | | |
| DEX0374_48 .nt.1 | SEQID NO. 191 | CLASP2 | LIV .0081 | | | | |
| DEX0374_48 .nt.2 | SEQID NO. 192 | CLASP2 | LIV .0081 | | | | |
| DEX0374_49 .nt.1 | SEQID NO. 194 | CLASP2 | LIV .0048 | | | | |
| DEX0374_50 | SEQID | CLASP5 | LIV | | | | |

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| .nt.1 | NO. 196 | CLASP1 | .0057 | | | | |
| DEX0374_51 .nt.1 | SEQID NO. 198 | CLASP2 | LIV .0048 | | | | |
| DEX0374_52 .nt.1 | SEQID NO. 201 | CLASP2 | LIV .0081 | | | | |
| DEX0374_53 .nt.1 | SEQID NO. 203 | CLASP2 CLASP1 | LIV .0122 | BRN .0001 | FTS .0001 | | |
| DEX0374_53 .nt.2 | SEQID NO. 204 | CLASP2 CLASP1 | LIV .0122 | BRN .0001 | FTS .0001 | | |
| DEX0374_54 .nt.1 | SEQID NO. 229 | CLASP2 CLASP1 | LIV .0144 | FTS .0001 | | | |
| DEX0374_55 .nt.1 | SEQID NO. 231 | CLASP2 | LIV .0081 | ADR .0034 | | | |
| DEX0374_56 .nt.1 | SEQID NO. 233 | CLASP2 | LIV .0081 | | | | |
| DEX0374_56 .nt.2 | SEQID NO. 234 | CLASP2 | LIV .0081 | | | | |
| DEX0374_57 .nt.1 | SEQID NO. 246 | CLASP2 | LIV .0048 | | | | |
| DEX0374_58 .nt.1 | SEQID NO. 248 | CLASP1 | LIV .0032 | FTS .0001 | | | |
| DEX0374_59 .nt.1 | SEQID NO. 250 | CLASP2 | LIV .0081 | URE .0078 | | | |
| DEX0374_60 .nt.1 | SEQID NO. 252 | CLASP5 CLASP1 | LIV .0132 | INL .0004 | FTS .0007 | KID .0012 | KID .0026 |
| DEX0374_60 .nt.2 | SEQID NO. 253 | CLASP5 CLASP1 | LIV .0132 | INL .0004 | FTS .0007 | KID .0012 | KID .0026 |
| DEX0374_61 .nt.1 | SEQID NO. 255 | CLASP5 CLASP1 | LIV .0057 | MAM .0008 | | | |
| DEX0374_62 .nt.1 | SEQID NO. 257 | CLASP2 | LIV .0129 | | | | |
| DEX0374_63 .nt.1 | SEQID NO. 259 | CLASP1 | LIV .0032 | FTS .0001 | UTR .0004 | | |
| DEX0374_63 .nt.2 | SEQID NO. 260 | CLASP1 | LIV .0032 | FTS .0001 | UTR .0004 | | |
| DEX0374_64 .nt.1 | SEQID NO. 262 | CLASP2 | LIV .0081 | | | | |
| DEX0374_64 .nt.2 | SEQID NO. 263 | CLASP2 | LIV .0081 | | | | |

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|---------------------|---------------------|------------------|--------------|--------------|--------------|--------------|--------------|
| DEX0374_65 .nt.1 | SEQID NO. 265 | CLASP1 | LIV .0032 | BRN .0003 | FTS .0005 | | |
| DEX0374_65 .nt.2 | SEQID NO. 266 | CLASP1 | LIV .0032 | BRN .0003 | FTS .0005 | | |
| DEX0374_66 .nt.1 | SEQID NO. 268 | CLASP2 CLASP1 | LIV .0122 | KID .0006 | OVR .0007 | GLB .0041 | |
| DEX0374_67 .nt.1 | SEQID NO. 270 | CLASP2 CLASP1 | LIV .0122 | MAM .0004 | | | |
| DEX0374_68 .nt.1 | SEQID NO. 272 | CLASP2 | LIV .0048 | | | | |
| DEX0374_69 .nt.1 | SEQID NO. 274 | CLASP1 | LIV .0032 | FTS .0001 | BRN .0004 | INL .0008 | UNC .0011 |
| DEX0374_69 .nt.2 | SEQID NO. 275 | CLASP1 | LIV .0032 | FTS .0001 | BRN .0004 | INL .0008 | UNC .0011 |
| DEX0374_70 .nt.1 | SEQID NO. 277 | CLASP2 | LIV .0081 | | | | |
| DEX0374_71 .nt.1 | SEQID NO. 280 | CLASP2 | LIV .0081 | | | | |
| DEX0374_71 .nt.2 | SEQID NO. 281 | CLASP2 | LIV .0081 | | | | |
| DEX0374_72 .nt.1 | SEQID NO. 283 | CLASP1 | LIV .0032 | | | | |
| DEX0374_73 .nt.1 | SEQID NO. 284 | CLASP2 | LIV .0129 | | | | |
| DEX0374_73 .nt.2 | SEQID NO. 285 | CLASP5 | | LMN .0028 | LNG .0034 | SPL .0063 | UNC .016 |
| DEX0374_74 .nt.1 | SEQID NO. 297 | CLASP2 | LIV .0081 | MAM .0019 | | | |
| DEX0374_75 .nt.1 | SEQID NO. 299 | CLASP5 CLASP1 | LIV .0094 | FTS .0001 | INL .0004 | CRD .002 | |
| DEX0374_76 .nt.1 | SEQID NO. 301 | CLASP2 | LIV .0081 | | | | |
| DEX0374_76 .nt.2 | SEQID NO. 302 | CLASP2 | LIV .0081 | | | | |
| DEX0374_77 .nt.1 | SEQID NO. 303 | CLASP2 | LIV .0048 | | | | |
| DEX0374_78 .nt.1 | SEQID NO. 305 | CLASP2 | LIV .0129 | | | | |
| DEX0374_79 .nt.1 | SEQID NO. | CLASP2 | LIV .0129 | MAM .0009 | | | |

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| | 307 | | | | | | |
| DEX0374_80 .nt.1 | SEQID NO. 309 | CLASP1 | LIV .0032 | FTS .0001 | | | |
| DEX0374_81 .nt.1 | SEQID NO. 329 | CLASP1 | LIV .0032 | | | | |
| DEX0374_82 .nt.1 | SEQID NO. 331 | CLASP5 CLASP1 | LIV .013 | FTS .0005 | LMN .0034 | ESO .0039 | GLB .0041 |
| DEX0374_82 .nt.2 | SEQID NO. 332 | CLASP5 CLASP1 | LIV .013 | FTS .0005 | LMN .0034 | ESO .0039 | GLB .0041 |
| DEX0374_82 .nt.3 | SEQID NO. 333 | CLASP5 CLASP1 | LIV .013 | FTS .0005 | LMN .0034 | ESO .0039 | GLB .0041 |
| DEX0374_82 .nt.4 | SEQID NO. 334 | CLASP5 CLASP1 | LIV .013 | FTS .0005 | LMN .0034 | ESO .0039 | GLB .0041 |
| DEX0374_82 .nt.5 | SEQID NO. 335 | CLASP5 CLASP1 | LIV .013 | FTS .0005 | LMN .0034 | ESO .0039 | GLB .0041 |
| DEX0374_83 .nt.1 | SEQID NO. 341 | CLASP2 | LIV .0081 | LNG .0014 | | | |
| DEX0374_83 .nt.2 | SEQID NO. 342 | CLASP2 | LIV .0081 | LNG .0014 | | | |
| DEX0374_84 .nt.1 | SEQID NO. 344 | CLASP2 | LIV .0048 | | | | |
| DEX0374_85 .nt.1 | SEQID NO. 346 | CLASP2 | LIV .0048 | | | | |
| DEX0374_86 .nt.1 | SEQID NO. 379 | CLASP1 | LIV .0032 | UNC .0011 | | | |
| DEX0374_87 .nt.1 | SEQID NO. 381 | CLASP2 | LIV .0081 | | | | |
| DEX0374_88 .nt.1 | SEQID NO. 383 | CLASP2 | LIV .0081 | NOS .0287 | | | |
| DEX0374_88 .nt.2 | SEQID NO. 384 | CLASP5 | | PNS .0023 | ESO .0102 | | |
| DEX0374_89 .nt.1 | SEQID NO. 387 | CLASP2 | LIV .0129 | | | | |
| DEX0374_90 .nt.1 | SEQID NO. 389 | CLASP2 | LIV .0048 | | | | |
| DEX0374_91 .nt.1 | SEQID NO. 391 | CLASP2 | LIV .0048 | | | | |
| DEX0374_91 .nt.2 | SEQID NO. 392 | CLASP2 | LIV .0048 | | | | |
| DEX0374_92 | SEQID | CLASP2 | LIV | LNG | | | |

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|----------------------|---------------------|----------------------------|--------------|--------------|--------------|--------------|--------------|
| .nt.1 | NO. 394 | | .0081 | .001 | | | |
| DEX0374_93 .nt.1 | SEQID NO. 396 | CLASP2 | LIV .0048 | | | | |
| DEX0374_94 .nt.1 | SEQID NO. 398 | CLASP2 | LIV .0065 | OVR .0028 | | | |
| DEX0374_95 .nt.1 | SEQID NO. 400 | CLASP2 | LIV .0081 | INL .0031 | | | |
| DEX0374_96 .nt.1 | SEQID NO. 402 | CLASP2 CLASP1 | LIV .0144 | FTS .0001 | | | |
| DEX0374_97 .nt.1 | SEQID NO. 403 | CLASP2 CLASP1 | LIV .0144 | FTS .0001 | | | |
| DEX0374_98 .nt.1 | SEQID NO. 404 | CLASP5 CLASP1 CLASP4 | LIV .0529 | BRN .0003 | BRN .0004 | UTR .0004 | UTR .0006 |
| DEX0374_99 .nt.1 | SEQID NO. 405 | CLASP1 | LIV .0032 | SKN .0015 | STO .0021 | | |
| DEX0374_10 0.nt.1 | SEQID NO. 406 | CLASP2 | LIV .0081 | CON .0016 | | | |
| DEX0374_10 1.nt.1 | SEQID NO. 407 | CLASP5 CLASP3 | LIV .0019 | THY .002 | PNS .0023 | PAN .0024 | TST .0027 |
| DEX0374_10 2.nt.1 | SEQID NO. 408 | CLASP2 | LIV .0129 | | | | |
| DEX0374_10 3.nt.1 | SEQID NO. 409 | CLASP2 | LIV .0081 | | | | |

Abbreviation for tissues:

- 5 ADR Adrenal Glands, BLD Bladder, BLO Blood, BLV Blood Vessels, BRN Brain, CON Connective Tissue, ESO Esophagus, FTS Fetus, INL Intestine, Large, INS Intestine, Small, LNG Lung, MAM Breast, NRV Nervous Tissue, OVR Ovary, PAN Pancreas, PNS Penis, PRO Prostate, SPL Spleen, STO Stomach, SYN Synovial Membranes, THR Thyroid Gland, THY Thymus Gland, UNC Mixed Tissues, UTR Uterus

- 10 The mapping of the nucleic acid ("NT") SEQ ID NO; DEX ID; chromosomal location (if known); open reading frame (ORF) location; amino acid ("AA") SEQ ID NO and AA DEX ID are shown in the table below:

| NT SEQ_No | NT_SEQID | Chromo Map | ORF_Loc | AA SEQ_NO | AA_SEQID |
|--------------|----------------|---------------|---------|--------------|----------------|
| 1 | DEX0374_1.nt.1 | 13q14.11 | | | |
| 2 | DEX0374_1.nt.2 | 13q14.11 | - | | |
| 3 | DEX0374_2.nt.1 | * | | 410 | DEX0374_2.aa.1 |
| 4 | DEX0374_2.nt.2 | * | - | | |
| 5 | DEX0374_3.nt.1 | 7p14.1 | | 411 | DEX0374_3.aa.1 |
| 6 | DEX0374_3.nt.2 | 7p14.1 | 29-2594 | 412 | DEX0374_3.aa.2 |
| 7 | DEX0374_3.nt.3 | 7p14.1 | - | | |

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| 8 | DEX0374 3.nt.4 | 7p14.1 | 29-2594 | 412 | DEX0374 3.aa.2 |
| 9 | DEX0374 3.nt.5 | 7p14.1 | 29-2594 | 412 | DEX0374 3.aa.2 |
| 10 | DEX0374 3.nt.6 | 7p14.1 | 232-1410 | 413 | DEX0374 3.aa.6 |
| 11 | DEX0374 3.nt.7 | 7p14.1 | - | | |
| 12 | DEX0374 3.nt.8 | 7p14.1 | - | | |
| 13 | DEX0374 3.nt.9 | 7p14.1 | 29-2438 | 414 | DEX0374 3.aa.9 |
| 14 | DEX0374 3.nt.10 | 7p14.1 | - | | |
| 15 | DEX0374 3.nt.11 | 7p14.1 | 29-2594 | 412 | DEX0374 3.aa.2 |
| 16 | DEX0374 3.nt.12 | 7p14.1 | 29-2555 | 415 | DEX0374 3.aa.12 |
| 17 | DEX0374 3.nt.13 | 7p14.1 | 29-2358 | 416 | DEX0374 3.aa.13 |
| 18 | DEX0374 3.nt.14 | 7p14.1 | 29-1277 | 417 | DEX0374 3.aa.14 |
| 19 | DEX0374 3.nt.15 | 7p14.1 | 29-1070 | 418 | DEX0374 3.aa.15 |
| 20 | DEX0374 3.nt.16 | 7p14.1 | 29-506 | 419 | DEX0374 3.aa.16 |
| 21 | DEX0374 3.nt.17 | 7p14.1 | - | | |
| 22 | DEX0374 3.nt.18 | 7p14.1 | 29-2594 | 412 | DEX0374 3.aa.2 |
| 23 | DEX0374 3.nt.19 | 7p14.1 | 466-2805 | 420 | DEX0374 3.aa.19 |
| 24 | DEX0374 3.nt.20 | 7p14.1 | 29-2594 | 412 | DEX0374 3.aa.2 |
| 25 | DEX0374 3.nt.21 | 7p14.1 | 29-2594 | 412 | DEX0374 3.aa.2 |
| 26 | DEX0374 3.nt.22 | 7p14.1 | 29-2651 | 421 | DEX0374 3.aa.22 |
| 27 | DEX0374 3.nt.23 | 7p14.1 | 29-2510 | 422 | DEX0374 3.aa.23 |
| 28 | DEX0374 3.nt.24 | 7p14.1 | 29-1583 | 423 | DEX0374 3.aa.24 |
| 29 | DEX0374 3.nt.25 | 7p14.1 | 29-839 | 424 | DEX0374 3.aa.25 |
| 30 | DEX0374 4.nt.1 | 3p26.2 | | 425 | DEX0374 4.aa.1 |
| 31 | DEX0374 4.nt.2 | 3p26.2 | - | | |
| 32 | DEX0374 5.nt.1 | 10q22.3 | | 426 | DEX0374 5.aa.1 |
| 33 | DEX0374 5.nt.2 | 10q22.3 | - | | |
| 34 | DEX0374 6.nt.1 | 13q12.11 | | | |
| 35 | DEX0374 6.nt.2 | 13q12.11 | - | | |
| 36 | DEX0374 6.nt.3 | 13q12.11 | 1-173 | 427 | DEX0374 6.aa.3 |
| 37 | DEX0374 6.nt.4 | 13q12.11 | - | | |
| 38 | DEX0374 6.nt.5 | 13q12.11 | 70-1023 | 428 | DEX0374 6.aa.5 |
| 39 | DEX0374 6.nt.6 | 13q12.11 | - | | |
| 40 | DEX0374 6.nt.7 | 13q12.11 | - | | |
| 41 | DEX0374 6.nt.8 | 13q12.11 | - | | |
| 42 | DEX0374 6.nt.9 | 13q12.11 | - | | |
| 43 | DEX0374 6.nt.10 | 13q12.11 | 70-1344 | 429 | DEX0374 6.aa.10 |
| 44 | DEX0374 6.nt.11 | 13q12.11 | 70-1053 | 430 | DEX0374 6.aa.11 |
| 45 | DEX0374 6.nt.12 | 13q12.11 | 70-681 | 431 | DEX0374 6.aa.12 |
| 46 | DEX0374 6.nt.13 | 13q12.11 | - | | |
| 47 | DEX0374 6.nt.14 | 13q12.11 | - | | |
| 48 | DEX0374 6.nt.15 | 13q12.11 | 1-533 | 432 | DEX0374 6.aa.15 |
| 49 | DEX0374 6.nt.16 | 13q12.11 | 70-1401 | 433 | DEX0374 6.aa.16 |
| 50 | DEX0374 6.nt.17 | 13q12.11 | 70-1218 | 434 | DEX0374 6.aa.17 |
| 51 | DEX0374 7.nt.1 | 1p32.2 | | 435 | DEX0374 7.aa.1 |
| 52 | DEX0374 7.nt.2 | 1p32.2 | - | | |
| 53 | DEX0374 8.nt.1 | 3q29 | | 436 | DEX0374 8.aa.1 |
| 54 | DEX0374 8.nt.2 | 3q29 | | | |
| 55 | DEX0374 8.nt.3 | 3q29 | - | | |
| 56 | DEX0374 9.nt.1 | 1p32.3 | | 437 | DEX0374 9.aa.1 |
| 57 | DEX0374 9.nt.2 | 1p32.3 | - | | |
| 58 | DEX0374 10.nt.1 | 7q33 | | 438 | DEX0374 10.aa.1 |
| 59 | DEX0374 10.nt.2 | 7q33 | - | | |
| 60 | DEX0374 11.nt.1 | 5q12.3 | | 439 | DEX0374 11.aa.1 |
| 61 | DEX0374 11.nt.2 | 5q12.3 | - | | |
| 62 | DEX0374 11.nt.3 | 5q12.3 | - | | |
| 63 | DEX0374 11.nt.4 | 5q12.3 | - | | |
| 64 | DEX0374 11.nt.5 | 5q12.3 | - | | |

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| 65 | DEX0374 12.nt.1 | 3p22.1 | | 440 | DEX0374 12.aa.1 |
| 66 | DEX0374 12.nt.2 | 3p22.1 | - | | |
| 67 | DEX0374 13.nt.1 | 6q14.1 | | 441 | DEX0374 13.aa.1 |
| 68 | DEX0374 13.nt.2 | 6q14.1 | - | | |
| 69 | DEX0374 14.nt.1 | 14q22.2 | | 442 | DEX0374 14.aa.1 |
| 70 | DEX0374 15.nt.1 | 1q24.3 | | 443 | DEX0374 15.aa.1 |
| 71 | DEX0374 15.nt.2 | 1q24.3 | | | |
| 72 | DEX0374 15.nt.3 | 1q24.3 | - | | |
| 73 | DEX0374 16.nt.1 | 14q13.2 | | 444 | DEX0374 16.aa.1 |
| 74 | DEX0374 16.nt.2 | 14q13.2 | | | |
| 75 | DEX0374 16.nt.3 | * | - | | |
| 76 | DEX0374 16.nt.4 | * | 73-2941 | 445 | DEX0374 16.aa.4 |
| 77 | DEX0374 16.nt.5 | * | - | | |
| 78 | DEX0374 16.nt.6 | * | 73-5737 | 446 | DEX0374 16.aa.6 |
| 79 | DEX0374 16.nt.7 | * | 513-4881 | 447 | DEX0374 16.aa.7 |
| 80 | DEX0374 16.nt.8 | * | 73-5389 | 448 | DEX0374 16.aa.8 |
| 81 | DEX0374 16.nt.9 | * | 16-4229 | 449 | DEX0374 16.aa.9 |
| 82 | DEX0374 16.nt.10 | * | 73-5737 | 446 | DEX0374 16.aa.6 |
| 83 | DEX0374 16.nt.11 | * | 73-5803 | 450 | DEX0374 16.aa.11 |
| 84 | DEX0374 16.nt.12 | * | 73-5737 | 446 | DEX0374 16.aa.6 |
| 85 | DEX0374 16.nt.13 | * | - | | |
| 86 | DEX0374 16.nt.14 | * | - | | |
| 87 | DEX0374 16.nt.15 | * | 73-5737 | 446 | DEX0374 16.aa.6 |
| 88 | DEX0374 16.nt.16 | * | 73-5186 | 451 | DEX0374 16.aa.16 |
| 89 | DEX0374 16.nt.17 | * | 73-3793 | 452 | DEX0374 16.aa.17 |
| 90 | DEX0374 16.nt.18 | * | 73-2623 | 453 | DEX0374 16.aa.18 |
| 91 | DEX0374 16.nt.19 | * | - | | |
| 92 | DEX0374 16.nt.20 | * | 73-928 | 454 | DEX0374 16.aa.20 |
| 93 | DEX0374 16.nt.21 | * | 73-1897 | 455 | DEX0374 16.aa.21 |
| 94 | DEX0374 16.nt.22 | * | 73-5878 | 456 | DEX0374 16.aa.22 |
| 95 | DEX0374 16.nt.23 | * | 572-4235 | 457 | DEX0374 16.aa.23 |
| 96 | DEX0374 16.nt.24 | * | 73-3454 | 458 | DEX0374 16.aa.24 |
| 97 | DEX0374 16.nt.25 | * | 73-5758 | 459 | DEX0374 16.aa.25 |
| 98 | DEX0374 16.nt.26 | * | 73-5677 | 460 | DEX0374 16.aa.26 |
| 99 | DEX0374 16.nt.27 | * | 73-5794 | 461 | DEX0374 16.aa.27 |
| 100 | DEX0374 16.nt.28 | * | 73-5743 | 462 | DEX0374 16.aa.28 |
| 101 | DEX0374 16.nt.29 | * | 73-2657 | 463 | DEX0374 16.aa.29 |
| 102 | DEX0374 16.nt.30 | * | 73-1366 | 464 | DEX0374 16.aa.30 |
| 103 | DEX0374 16.nt.31 | * | 73-1324 | 465 | DEX0374 16.aa.31 |
| 104 | DEX0374 17.nt.1 | 16q21 | | 466 | DEX0374 17.aa.1 |
| 105 | DEX0374 17.nt.2 | 16q21 | - | | |
| 106 | DEX0374 17.nt.3 | 16q21 | 301-898 | 467 | DEX0374 17.aa.3 |
| 107 | DEX0374 17.nt.4 | 16q21 | 66-867 | 468 | DEX0374 17.aa.4 |
| 108 | DEX0374 17.nt.5 | 16q21 | 301-1054 | 469 | DEX0374 17.aa.5 |
| 109 | DEX0374 17.nt.6 | 16q21 | 43-310 | 470 | DEX0374 17.aa.6 |
| 110 | DEX0374 17.nt.7 | 16q21 | 301-823 | 471 | DEX0374 17.aa.7 |
| 111 | DEX0374 17.nt.8 | 16q21 | 301-823 | 471 | DEX0374 17.aa.7 |
| 112 | DEX0374 17.nt.9 | 16q21 | 392-725 | 472 | DEX0374 17.aa.9 |
| 113 | DEX0374 18.nt.1 | 14q32.32 | | 473 | DEX0374 18.aa.1 |
| 114 | DEX0374 18.nt.2 | 14q32.32 | | | |
| 115 | DEX0374 18.nt.3 | 14q32.32 | - | | |
| 116 | DEX0374 18.nt.4 | * | - | | |
| 117 | DEX0374 19.nt.1 | 14q32.32 | | 474 | DEX0374 19.aa.1 |
| 118 | DEX0374 19.nt.2 | 14q32.32 | - | | |
| 119 | DEX0374 20.nt.1 | 2q31.1 | | 475 | DEX0374 20.aa.1 |
| 120 | DEX0374 20.nt.2 | 2q31.1 | | | |
| 121 | DEX0374 21.nt.1 | 10p12.33 | | 476 | DEX0374 21.aa.1 |

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|-----|-----------------|----------|-----------|-----|-----------------|
| 122 | DEX0374 21.nt.2 | 10p12.33 | - | | |
| 123 | DEX0374 22.nt.1 | 11p13 | | 477 | DEX0374 22.aa.1 |
| 124 | DEX0374 22.nt.2 | 11p13 | | | |
| 125 | DEX0374 22.nt.3 | 11p13 | - | | |
| 126 | DEX0374 23.nt.1 | 1q31.3 | | 478 | DEX0374 23.aa.1 |
| 127 | DEX0374 23.nt.2 | 1q31.3 | | | |
| 128 | DEX0374 23.nt.3 | 1q31.3 | - | | |
| 129 | DEX0374 23.nt.4 | 1q31.3 | - | | |
| 130 | DEX0374 23.nt.5 | 1q31.3 | - | | |
| 131 | DEX0374 24.nt.1 | 16p13.3 | | 479 | DEX0374 24.aa.1 |
| 132 | DEX0374 24.nt.2 | 16p13.3 | 629-1727 | 480 | DEX0374 24.aa.2 |
| 133 | DEX0374 24.nt.3 | 16p13.3 | 1215-2214 | 481 | DEX0374 24.aa.3 |
| 134 | DEX0374 25.nt.1 | * | | 482 | DEX0374 25.aa.1 |
| 135 | DEX0374 25.nt.2 | * | - | | |
| 136 | DEX0374 26.nt.1 | Xp11.23 | | | |
| 137 | DEX0374 27.nt.1 | 16q24.3 | | 483 | DEX0374 27.aa.1 |
| 138 | DEX0374 27.nt.2 | 16q24.3 | 1-199 | 484 | DEX0374 27.aa.2 |
| 139 | DEX0374 28.nt.1 | 10p12.1 | | 485 | DEX0374 28.aa.1 |
| 140 | DEX0374 28.nt.2 | 10p12.1 | | | |
| 141 | DEX0374 28.nt.3 | 10p12.1 | - | | |
| 142 | DEX0374 29.nt.1 | 2p13.1 | | 486 | DEX0374 29.aa.1 |
| 143 | DEX0374 29.nt.2 | 2p13.1 | | | |
| 144 | DEX0374 29.nt.3 | 2p13.1 | - | | |
| 145 | DEX0374 30.nt.1 | 1q23.3 | | 487 | DEX0374 30.aa.1 |
| 146 | DEX0374 30.nt.2 | 1q23.3 | - | | |
| 147 | DEX0374 31.nt.1 | 1p34.3 | | 488 | DEX0374 31.aa.1 |
| 148 | DEX0374 31.nt.2 | 1p34.3 | | | |
| 149 | DEX0374 31.nt.3 | 1p34.3 | - | | |
| 150 | DEX0374 32.nt.1 | Xp21.1 | | 489 | DEX0374 32.aa.1 |
| 151 | DEX0374 32.nt.2 | Xp21.1 | - | | |
| 152 | DEX0374 33.nt.1 | 1q31.3 | | 490 | DEX0374 33.aa.1 |
| 153 | DEX0374 33.nt.2 | 1q31.3 | - | | |
| 154 | DEX0374 34.nt.1 | 6p22.2 | | 491 | DEX0374 34.aa.1 |
| 155 | DEX0374 34.nt.2 | 6p22.2 | - | | |
| 156 | DEX0374 34.nt.3 | 6p22.2 | - | | |
| 157 | DEX0374 35.nt.1 | 16q13 | | 492 | DEX0374 35.aa.1 |
| 158 | DEX0374 35.nt.2 | 16q13 | 75-546 | 493 | DEX0374 35.aa.2 |
| 159 | DEX0374 36.nt.1 | 12q23.3 | | 494 | DEX0374 36.aa.1 |
| 160 | DEX0374 36.nt.2 | 12q23.3 | - | | |
| 161 | DEX0374 36.nt.3 | * | - | | |
| 162 | DEX0374 37.nt.1 | 18q12.3 | | 495 | DEX0374 37.aa.1 |
| 163 | DEX0374 37.nt.2 | 18q12.3 | - | | |
| 164 | DEX0374 38.nt.1 | 17q21.31 | | 496 | DEX0374 38.aa.1 |
| 165 | DEX0374 38.nt.2 | 17q21.31 | | | |
| 166 | DEX0374 38.nt.3 | 17q21.31 | - | | |
| 167 | DEX0374 39.nt.1 | 20q11.23 | | 497 | DEX0374 39.aa.1 |
| 168 | DEX0374 39.nt.2 | 20q11.23 | | | |
| 169 | DEX0374 39.nt.3 | 20q11.23 | 1-134 | 498 | DEX0374 39.aa.3 |
| 170 | DEX0374 40.nt.1 | 14q23.3 | | 499 | DEX0374 40.aa.1 |
| 171 | DEX0374 40.nt.2 | 14q23.3 | - | | |
| 172 | DEX0374 41.nt.1 | * | | 500 | DEX0374 41.aa.1 |
| 173 | DEX0374 41.nt.2 | * | - | | |
| 174 | DEX0374 42.nt.1 | 14q23.3 | | 501 | DEX0374 42.aa.1 |
| 175 | DEX0374 42.nt.2 | 14q23.3 | - | | |
| 176 | DEX0374 43.nt.1 | * | | 502 | DEX0374 43.aa.1 |
| 177 | DEX0374 43.nt.2 | * | | | |

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| 178 | DEX0374 43.nt.3 | * | 179-560 | 503 | DEX0374 43.aa.3 |
| 179 | DEX0374 43.nt.4 | * | - | | |
| 180 | DEX0374 44.nt.1 | 16p12.3 | | 504 | DEX0374 44.aa.1 |
| 181 | DEX0374 44.nt.2 | 16p12.3 | - | | |
| 182 | DEX0374 45.nt.1 | 5q31.1 | | 505 | DEX0374 45.aa.1 |
| 183 | DEX0374 45.nt.2 | 5q31.1 | 157-583 | 506 | DEX0374 45.aa.2 |
| 184 | DEX0374 46.nt.1 | * | | 507 | DEX0374 46.aa.1 |
| 185 | DEX0374 46.nt.2 | * | - | | |
| 186 | DEX0374 47.nt.1 | 6q25.1 | | 508 | DEX0374 47.aa.1 |
| 187 | DEX0374 47.nt.2 | 6q25.1 | | 509 | DEX0374 47.aa.2 |
| 188 | DEX0374 47.nt.3 | 6q25.1 | | | |
| 189 | DEX0374 47.nt.4 | 6q25.1 | - | | |
| 190 | DEX0374 47.nt.5 | 6q25.1 | - | | |
| 191 | DEX0374 48.nt.1 | * | | 510 | DEX0374 48.aa.1 |
| 192 | DEX0374 48.nt.2 | * | | | |
| 193 | DEX0374 48.nt.3 | * | - | | |
| 194 | DEX0374 49.nt.1 | 18q12.3 | | 511 | DEX0374 49.aa.1 |
| 195 | DEX0374 49.nt.2 | 18q12.3 | - | | |
| 196 | DEX0374 50.nt.1 | 20q11.23 | | 512 | DEX0374 50.aa.1 |
| 197 | DEX0374 50.nt.2 | 20q11.23 | - | | |
| 198 | DEX0374 51.nt.1 | 2p23.3 | | 513 | DEX0374 51.aa.1 |
| 199 | DEX0374 51.nt.2 | 2p23.3 | - | | |
| 200 | DEX0374 51.nt.3 | 2p23.3 | - | | |
| 201 | DEX0374 52.nt.1 | 13q12.11 | | | |
| 202 | DEX0374 52.nt.2 | 13q12.11 | - | | |
| 203 | DEX0374 53.nt.1 | * | | 514 | DEX0374 53.aa.1 |
| 204 | DEX0374 53.nt.2 | * | | | |
| 205 | DEX0374 53.nt.3 | 16p11.2 | 82-2981 | 515 | DEX0374 53.aa.3 |
| 206 | DEX0374 53.nt.4 | 16p11.2 | 1-608 | 516 | DEX0374 53.aa.4 |
| 207 | DEX0374 53.nt.5 | 16p11.2 | - | | |
| 208 | DEX0374 53.nt.6 | 16p11.2 | 681-991 | 517 | DEX0374 53.aa.6 |
| 209 | DEX0374 53.nt.7 | 16p11.2 | 82-2958 | 518 | DEX0374 53.aa.7 |
| 210 | DEX0374 53.nt.8 | 16p11.2 | 82-2596 | 519 | DEX0374 53.aa.8 |
| 211 | DEX0374 53.nt.9 | 16p11.2 | 82-2596 | 519 | DEX0374 53.aa.8 |
| 212 | DEX0374 53.nt.10 | 16p11.2 | 91-1503 | 520 | DEX0374 53.aa.10 |
| 213 | DEX0374 53.nt.11 | 16p11.2 | 322-1079 | 521 | DEX0374 53.aa.11 |
| 214 | DEX0374 53.nt.12 | 16p11.2 | 82-2164 | 522 | DEX0374 53.aa.12 |
| 215 | DEX0374 53.nt.13 | 16p11.2 | 82-2176 | 523 | DEX0374 53.aa.13 |
| 216 | DEX0374 53.nt.14 | 16p11.2 | 133-889 | 524 | DEX0374 53.aa.14 |
| 217 | DEX0374 53.nt.15 | 16p11.2 | 82-1789 | 525 | DEX0374 53.aa.15 |
| 218 | DEX0374 53.nt.16 | 16p11.2 | 133-912 | 526 | DEX0374 53.aa.16 |
| 219 | DEX0374 53.nt.17 | 16p11.2 | 91-470 | 527 | DEX0374 53.aa.17 |
| 220 | DEX0374 53.nt.18 | 16p11.2 | 1-680 | 528 | DEX0374 53.aa.18 |
| 221 | DEX0374 53.nt.19 | 16p11.2 | 82-2836 | 529 | DEX0374 53.aa.19 |
| 222 | DEX0374 53.nt.20 | 16p11.2 | 82-2638 | 530 | DEX0374 53.aa.20 |
| 223 | DEX0374 53.nt.21 | 16p11.2 | 82-2861 | 531 | DEX0374 53.aa.21 |
| 224 | DEX0374 53.nt.22 | 16p11.2 | 82-3118 | 532 | DEX0374 53.aa.22 |
| 225 | DEX0374 53.nt.23 | 16p11.2 | 46-1018 | 533 | DEX0374 53.aa.23 |
| 226 | DEX0374 53.nt.24 | 16p11.2 | 1536-1844 | 517 | DEX0374 53.aa.6 |
| 227 | DEX0374 53.nt.25 | * | 196-1003 | 534 | DEX0374 53.aa.25 |
| 228 | DEX0374 53.nt.26 | * | 16-989 | 535 | DEX0374 53.aa.26 |
| 229 | DEX0374 54.nt.1 | 6q22.1 | | 536 | DEX0374 54.aa.1 |
| 230 | DEX0374 54.nt.2 | 6q22.1 | - | | |
| 231 | DEX0374 55.nt.1 | 9q31.1 | | 537 | DEX0374 55.aa.1 |
| 232 | DEX0374 55.nt.2 | 9q31.1 | - | | |
| 233 | DEX0374 56.nt.1 | 7q36.1 | | 538 | DEX0374 56.aa.1 |

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| 234 | DEX0374 56.nt.2 | 7q36.1 | | | |
| 235 | DEX0374 56.nt.3 | 7q36.1 | 1-361 | 539 | DEX0374 56.aa.3 |
| 236 | DEX0374 56.nt.4 | 7q36.1 | 366-1980 | 540 | DEX0374 56.aa.4 |
| 237 | DEX0374 56.nt.5 | 7q36.1 | 335-1949 | 540 | DEX0374 56.aa.4 |
| 238 | DEX0374 56.nt.6 | 7q36.1 | 126-1740 | 540 | DEX0374 56.aa.4 |
| 239 | DEX0374 56.nt.7 | 7q36.1 | 126-1740 | 540 | DEX0374 56.aa.4 |
| 240 | DEX0374 56.nt.8 | 7q36.1 | - | | |
| 241 | DEX0374 56.nt.9 | 7q36.1 | 487-694 | 541 | DEX0374 56.aa.9 |
| 242 | DEX0374 56.nt.10 | 7q36.1 | 126-1740 | 540 | DEX0374 56.aa.4 |
| 243 | DEX0374 56.nt.11 | 7q36.1 | 487-2101 | 540 | DEX0374 56.aa.4 |
| 244 | DEX0374 56.nt.12 | 7q36.1 | 132-1785 | 542 | DEX0374 56.aa.12 |
| 245 | DEX0374 56.nt.13 | 7q36.1 | 126-723 | 543 | DEX0374 56.aa.13 |
| 246 | DEX0374 57.nt.1 | 6q22.1 | | 544 | DEX0374 57.aa.1 |
| 247 | DEX0374 57.nt.2 | 6q22.1 | - | | |
| 248 | DEX0374 58.nt.1 | 13q34 | | 545 | DEX0374 58.aa.1 |
| 249 | DEX0374 58.nt.2 | 13q34 | - | | |
| 250 | DEX0374 59.nt.1 | 3p14.1 | | 546 | DEX0374 59.aa.1 |
| 251 | DEX0374 59.nt.2 | 3p14.1 | - | | |
| 252 | DEX0374 60.nt.1 | 10q11.23 | | 547 | DEX0374 60.aa.1 |
| 253 | DEX0374 60.nt.2 | 10q11.23 | | | |
| 254 | DEX0374 60.nt.3 | 10q11.23 | 22-371 | 548 | DEX0374 60.aa.3 |
| 255 | DEX0374 61.nt.1 | 1q31.3 | | 549 | DEX0374 61.aa.1 |
| 256 | DEX0374 61.nt.2 | 1q31.3 | - | | |
| 257 | DEX0374 62.nt.1 | 17q25.3 | | 550 | DEX0374 62.aa.1 |
| 258 | DEX0374 62.nt.2 | 17q25.3 | - | | |
| 259 | DEX0374 63.nt.1 | 1q25.1 | | 551 | DEX0374 63.aa.1 |
| 260 | DEX0374 63.nt.2 | 1q25.1 | | | |
| 261 | DEX0374 63.nt.3 | 1q25.1 | - | | |
| 262 | DEX0374 64.nt.1 | 14q12 | | 552 | DEX0374 64.aa.1 |
| 263 | DEX0374 64.nt.2 | 14q12 | | | |
| 264 | DEX0374 64.nt.3 | 14q12 | - | | |
| 265 | DEX0374 65.nt.1 | 16p12.1 | | 553 | DEX0374 65.aa.1 |
| 266 | DEX0374 65.nt.2 | 16p12.1 | | | |
| 267 | DEX0374 65.nt.3 | 16p12.1 | - | | |
| 268 | DEX0374 66.nt.1 | 16q13 | | 554 | DEX0374 66.aa.1 |
| 269 | DEX0374 66.nt.2 | 16q13 | - | | |
| 270 | DEX0374 67.nt.1 | 19q13.31 | | 555 | DEX0374 67.aa.1 |
| 271 | DEX0374 67.nt.2 | 19q13.31 | - | | |
| 272 | DEX0374 68.nt.1 | 3q29 | | 556 | DEX0374 68.aa.1 |
| 273 | DEX0374 68.nt.2 | 3q29 | - | | |
| 274 | DEX0374 69.nt.1 | 8q12.3 | | 557 | DEX0374 69.aa.1 |
| 275 | DEX0374 69.nt.2 | 8q12.3 | | | |
| 276 | DEX0374 69.nt.3 | 8q12.3 | - | | |
| 277 | DEX0374 70.nt.1 | 5q33.1 | | 558 | DEX0374 70.aa.1 |
| 278 | DEX0374 70.nt.2 | 5q33.1 | 1-180 | 559 | DEX0374 70.aa.2 |
| 279 | DEX0374 70.nt.3 | 5q33.1 | 1-168 | 560 | DEX0374 70.aa.3 |
| 280 | DEX0374 71.nt.1 | 16q13 | | 561 | DEX0374 71.aa.1 |
| 281 | DEX0374 71.nt.2 | 16q13 | | | |
| 282 | DEX0374 71.nt.3 | 16q13 | - | | |
| 283 | DEX0374 72.nt.1 | 6p21.1 | | 562 | DEX0374 72.aa.1 |
| 284 | DEX0374 73.nt.1 | 12p13.33 | | 563 | DEX0374 73.aa.1 |
| 285 | DEX0374 73.nt.2 | 12p13.33 | | | |
| 286 | DEX0374 73.nt.3 | 12p13.33 | 1-966 | 564 | DEX0374 73.aa.3 |
| 287 | DEX0374 73.nt.4 | 12p13.33 | 1-966 | 564 | DEX0374 73.aa.3 |
| 288 | DEX0374 73.nt.5 | 12p13.33 | 1-966 | 564 | DEX0374 73.aa.3 |
| 289 | DEX0374 73.nt.6 | 12p13.33 | 1-966 | 564 | DEX0374 73.aa.3 |
| 290 | DEX0374 73.nt.7 | 12p13.33 | 1-966 | 564 | DEX0374 73.aa.3 |

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|-----|------------------|----------|-----------|-----|------------------|
| 291 | DEX0374 73.nt.8 | 12p13.33 | 737-1187 | 565 | DEX0374 73.aa.8 |
| 292 | DEX0374 73.nt.9 | 12p13.33 | 592-1756 | 566 | DEX0374 73.aa.9 |
| 293 | DEX0374 73.nt.10 | 12p13.33 | - | | |
| 294 | DEX0374 73.nt.11 | 12p13.33 | 1-97 | 567 | DEX0374 73.aa.11 |
| 295 | DEX0374 73.nt.12 | 12p13.33 | 592-1129 | 568 | DEX0374 73.aa.12 |
| 296 | DEX0374 73.nt.13 | 12p13.33 | - | | |
| 297 | DEX0374 74.nt.1 | 1q32.1 | | 569 | DEX0374 74.aa.1 |
| 298 | DEX0374 74.nt.2 | 1q32.1 | - | | |
| 299 | DEX0374 75.nt.1 | 11q23.2 | | | |
| 300 | DEX0374 75.nt.2 | 11q23.2 | - | | |
| 301 | DEX0374 76.nt.1 | 3q29 | | 570 | DEX0374 76.aa.1 |
| 302 | DEX0374 76.nt.2 | 3q29 | | | |
| 303 | DEX0374 77.nt.1 | 11q21 | | 571 | DEX0374 77.aa.1 |
| 304 | DEX0374 77.nt.2 | 11q21 | - | | |
| 305 | DEX0374 78.nt.1 | 9p21.2 | | 572 | DEX0374 78.aa.1 |
| 306 | DEX0374 78.nt.2 | * | - | | |
| 307 | DEX0374 79.nt.1 | 3q29 | | 573 | DEX0374 79.aa.1 |
| 308 | DEX0374 79.nt.2 | 3q29 | - | | |
| 309 | DEX0374 80.nt.1 | 13q14.13 | | 574 | DEX0374 80.aa.1 |
| 310 | DEX0374 80.nt.2 | * | 228-2415 | 575 | DEX0374 80.aa.2 |
| 311 | DEX0374 80.nt.3 | * | - | | |
| 312 | DEX0374 80.nt.4 | * | - | | |
| 313 | DEX0374 80.nt.5 | * | 228-2193 | 576 | DEX0374 80.aa.5 |
| 314 | DEX0374 80.nt.6 | * | - | | |
| 315 | DEX0374 80.nt.7 | * | 228-2319 | 577 | DEX0374 80.aa.7 |
| 316 | DEX0374 80.nt.8 | * | 31-209 | 578 | DEX0374 80.aa.8 |
| 317 | DEX0374 80.nt.9 | * | - | | |
| 318 | DEX0374 80.nt.10 | * | 1-198 | 579 | DEX0374 80.aa.10 |
| 319 | DEX0374 80.nt.11 | * | 228-2319 | 577 | DEX0374 80.aa.7 |
| 320 | DEX0374 80.nt.12 | * | - | | |
| 321 | DEX0374 80.nt.13 | * | 228-1839 | 580 | DEX0374 80.aa.13 |
| 322 | DEX0374 80.nt.14 | * | 228-1182 | 581 | DEX0374 80.aa.14 |
| 323 | DEX0374 80.nt.15 | * | 228-2319 | 577 | DEX0374 80.aa.7 |
| 324 | DEX0374 80.nt.16 | * | 73-612 | 582 | DEX0374 80.aa.16 |
| 325 | DEX0374 80.nt.17 | * | 228-2319 | 577 | DEX0374 80.aa.7 |
| 326 | DEX0374 80.nt.18 | * | 228-462 | 583 | DEX0374 80.aa.18 |
| 327 | DEX0374 80.nt.19 | * | 228-1737 | 584 | DEX0374 80.aa.19 |
| 328 | DEX0374 80.nt.20 | * | 228-684 | 585 | DEX0374 80.aa.20 |
| 329 | DEX0374 81.nt.1 | 8p11.21 | | 586 | DEX0374 81.aa.1 |
| 330 | DEX0374 81.nt.2 | 8p11.21 | - | | |
| 331 | DEX0374 82.nt.1 | * | | 587 | DEX0374 82.aa.1 |
| 332 | DEX0374 82.nt.2 | * | | | |
| 333 | DEX0374 82.nt.3 | * | | 588 | DEX0374 82.aa.3 |
| 334 | DEX0374 82.nt.4 | * | | 589 | DEX0374 82.aa.4 |
| 335 | DEX0374 82.nt.5 | * | | | |
| 336 | DEX0374 82.nt.6 | * | 1536-2034 | 590 | DEX0374 82.aa.6 |
| 337 | DEX0374 82.nt.7 | * | 37-606 | 591 | DEX0374 82.aa.7 |
| 338 | DEX0374 82.nt.8 | * | 37-606 | 591 | DEX0374 82.aa.7 |
| 339 | DEX0374 82.nt.9 | * | 109-370 | 592 | DEX0374 82.aa.9 |
| 340 | DEX0374 82.nt.10 | * | 37-606 | 591 | DEX0374 82.aa.7 |
| 341 | DEX0374 83.nt.1 | 1p34.1 | | | |
| 342 | DEX0374 83.nt.2 | 1p34.1 | | | |
| 343 | DEX0374 83.nt.3 | 1p34.1 | - | | |
| 344 | DEX0374 84.nt.1 | 2q21.3 | | 593 | DEX0374 84.aa.1 |
| 345 | DEX0374 84.nt.2 | 2q21.3 | - | | |
| 346 | DEX0374 85.nt.1 | 8p11.21 | | 594 | DEX0374 85.aa.1 |

| | | | | | |
|-----|------------------|---------|---------|-----|------------------|
| 347 | DEX0374 85.nt.2 | 8p11.21 | - | | |
| 348 | DEX0374 85.nt.3 | 8p11.21 | - | | |
| 349 | DEX0374 85.nt.4 | 8p11.21 | - | | |
| 350 | DEX0374 85.nt.5 | 8p11.21 | 139-424 | 595 | DEX0374 85.aa.5 |
| 351 | DEX0374 85.nt.6 | 8p11.21 | 121-405 | 596 | DEX0374 85.aa.6 |
| 352 | DEX0374 85.nt.7 | 8p11.21 | - | | |
| 353 | DEX0374 85.nt.8 | 8p11.21 | - | | |
| 354 | DEX0374 85.nt.9 | 8p11.21 | - | | |
| 355 | DEX0374 85.nt.10 | 8p11.21 | - | | |
| 356 | DEX0374 85.nt.11 | 8p11.21 | 1-249 | 597 | DEX0374 85.aa.11 |
| 357 | DEX0374 85.nt.12 | 8p11.21 | - | | |
| 358 | DEX0374 85.nt.13 | 8p11.21 | - | | |
| 359 | DEX0374 85.nt.14 | 8p11.21 | - | | |
| 360 | DEX0374 85.nt.15 | 8p11.21 | - | | |
| 361 | DEX0374 85.nt.16 | 8p11.21 | - | | |
| 362 | DEX0374 85.nt.17 | 8p11.21 | - | | |
| 363 | DEX0374 85.nt.18 | 8p11.21 | - | | |
| 364 | DEX0374 85.nt.19 | 8p11.21 | - | | |
| 365 | DEX0374 85.nt.20 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 366 | DEX0374 85.nt.21 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 367 | DEX0374 85.nt.22 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 368 | DEX0374 85.nt.23 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 369 | DEX0374 85.nt.24 | 8p11.21 | - | | |
| 370 | DEX0374 85.nt.25 | 8p11.21 | - | | |
| 371 | DEX0374 85.nt.26 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 372 | DEX0374 85.nt.27 | 8p11.21 | - | | |
| 373 | DEX0374 85.nt.28 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 374 | DEX0374 85.nt.29 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 375 | DEX0374 85.nt.30 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 376 | DEX0374 85.nt.31 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 377 | DEX0374 85.nt.32 | 8p11.21 | 1-436 | 598 | DEX0374 85.aa.20 |
| 378 | DEX0374 85.nt.33 | 8p11.21 | - | | |
| 379 | DEX0374 86.nt.1 | 11p15.5 | | 599 | DEX0374 86.aa.1 |
| 380 | DEX0374 86.nt.2 | 11p15.5 | 88-471 | 600 | DEX0374 86.aa.2 |
| 381 | DEX0374 87.nt.1 | 3q25.1 | | 601 | DEX0374 87.aa.1 |
| 382 | DEX0374 87.nt.2 | 3q25.1 | - | | |
| 383 | DEX0374 88.nt.1 | 1q42.2 | | 602 | DEX0374 88.aa.1 |
| 384 | DEX0374 88.nt.2 | 1q42.2 | | | |
| 385 | DEX0374 88.nt.3 | 1q42.2 | 254-659 | 603 | DEX0374 88.aa.3 |
| 386 | DEX0374 88.nt.4 | 1q42.2 | - | | |
| 387 | DEX0374 89.nt.1 | 1p32.1 | | 604 | DEX0374 89.aa.1 |
| 388 | DEX0374 89.nt.2 | 1p32.1 | - | | |
| 389 | DEX0374 90.nt.1 | 15q25.1 | | 605 | DEX0374 90.aa.1 |
| 390 | DEX0374 90.nt.2 | 15q25.1 | - | | |
| 391 | DEX0374 91.nt.1 | 1p21.3 | | 606 | DEX0374 91.aa.1 |
| 392 | DEX0374 91.nt.2 | 1p21.3 | | | |
| 393 | DEX0374 91.nt.3 | 1p21.3 | - | | |
| 394 | DEX0374 92.nt.1 | 13q33.1 | | | |
| 395 | DEX0374 92.nt.2 | 13q33.1 | - | | |
| 396 | DEX0374 93.nt.1 | 5q14.1 | | 607 | DEX0374 93.aa.1 |
| 397 | DEX0374 93.nt.2 | 5q14.1 | - | | |
| 398 | DEX0374 94.nt.1 | 2q35 | | 608 | DEX0374 94.aa.1 |
| 399 | DEX0374 94.nt.2 | 2q35 | - | | |
| 400 | DEX0374 95.nt.1 | 2q35 | | 609 | DEX0374 95.aa.1 |
| 401 | DEX0374 95.nt.2 | 2q35 | 1-417 | 610 | DEX0374 95.aa.2 |
| 402 | DEX0374 96.nt.1 | 6q22.1 | | | |
| 403 | DEX0374 97.nt.1 | 6q22.1 | | | |

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|-----|------------------|---------|--|-----|------------------|
| 404 | DEX0374 98.nt.1 | 12q23.3 | | | |
| 405 | DEX0374 99.nt.1 | 1p32.2 | | | |
| 406 | DEX0374 100.nt.1 | 9q31.3 | | 611 | DEX0374 100.aa.1 |
| 407 | DEX0374 101.nt.1 | 2q11.2 | | | |
| 408 | DEX0374 102.nt.1 | 7q22.1 | | | |
| 409 | DEX0374 103.nt.1 | * | | | |

For the polypeptides of the invention, the following attributes were found, epitopes, post translational modifications, signal peptides and transmembrane domains.

- 5 Antigenicity (Epitope) prediction was performed through the antigenic module in the EMBOSS package. Rice, P., EMBOSS: The European Molecular Biology Open Software Suite, *Trends in Genetics* 16(6): 276-277 (2000). The antigenic module predicts potentially antigenic regions of a protein sequence, using the method of Kolaskar and Tongaonkar. Kolaskar, AS and Tongaonkar, PC., A semi-empirical method for prediction of antigenic determinants on protein antigens, *FEBS Letters* 276: 172-174 (1990).
- 10 Examples of post-translational modifications (PTMs) and other motifs of the HSPs of this invention are listed below. In addition, antibodies that specifically bind such post-translational modifications may be useful as a diagnostic or as therapeutic. The PTMs and other motifs were predicted by using the ProSite Dictionary of Proteins Sites and Patterns (Bairoch *et al.*, *Nucleic Acids Res.* 25(1):217-221 (1997)), the following motifs, including
- 15 PTMs, were predicted for the HSPs of the invention. The signal peptides were detected by using the SignalP 2.0, *see* Nielsen *et al.*, *Protein Engineering* 12, 3-9 (1999). Prediction of transmembrane helices in proteins was performed by the application TMHMM 2.0, "currently the best performing transmembrane prediction program", according to authors
- 20 (Krogh *et al.*, *Journal of Molecular Biology*, 305(3):567-580, (2001); Moller *et al.*, *Bioinformatics*, 17(7):646-653, (2001); Sonnhammer, *et al.*, *A hidden Markov model for predicting transmembrane helices in protein sequences* in Glasgow, *et al.* Ed. Proceedings of the Sixth International Conference on Intelligent Systems for Molecular Biology, pages 175-182, Menlo Park, CA, 1998. AAI Press. The PSORT II program may also be used
- 25 to predict cellular localizations. Horton *et al.*, *Intelligent Systems for Molecular Biology* 5: 147-152 (1997). The table below includes the following sequence annotations: Signal peptide presence; TM (number of membrane domain, topology in orientation and position); Amino acid location and antigenic index (location, AI score, length); PTM and other motifs (type, amino acid residue locations).

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|--------------------|----------|-------|---|--|
| DEX0374_3. aa.2 | N | 0 -o | 268-290,1.26; 791-817,1.253; 237-246,1.216; 489-500,1.199; 44-73,1.187; 592- 604,1.181; 212- 233,1.172; 122- 146,1.171; 439- 471,1.17; 107- 114,1.165; 740- 774,1.16; 719- 729,1.16; 344- 358,1.159; 255- 265,1.137; 580- 586,1.135; 527- 551,1.132; 832- 840,1.132; 392- 408,1.127; 697- 712,1.12; 654- 661,1.12; 626- 651,1.117; 553- 561,1.117; 79- 90,1.113; 297- 317,1.107; 192- 198,1.104; 819- 825,1.1; 781- 788,1.094; 614- 623,1.093; 511- 520,1.092; 148- 155,1.082; 412- 421,1.08; 428- 436,1.079; 333- 339,1.074; 319- 325,1.071; 677- 686,1.066; 99- 105,1.066; 179- 185,1.057 | Amidation 152-155; Asn_Glycosylation 80- 83, 232-235, 494-497, 512-515; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16- 19, 20-23, 24-27, 29- 32, 57-60, 96-99, 120- 123, 247-250, 268-271, 299-302, 318-321, 345- 348, 355-358, 476-479, 518-521, 556-559, 724- 727; Myristyl 66-71, 117-122, 177-182, 445- 450, 669-674, 717-722; Pkc_Phospho_Site 82- 84, 145-147, 181-183, 217-219, 242-244, 247- 249, 296-298, 299-301, 328-330, 355-357, 390- 392, 538-540, 556-558, 569-571, 584-586, 844- 846; Rgd 413-415, 456-458; Tyr_Phospho_Site 517- 525, 655-663; |
| DEX0374_3. aa.6 | N | 0 -o | 329-355,1.253; 27-38,1.199; 130- 142,1.181; 278- 312,1.16; 257- 267,1.16; 118- 124,1.135; 65- 89,1.132; 370- 378,1.132; 235- 250,1.12; 192- 199,1.12; 164- 189,1.117; 91- 99,1.117; 357- 363,1.1; 319- 326,1.094; 152- 161,1.093; 49- 58,1.092; 215- 224,1.066 | Asn_Glycosylation 32- 35, 50-53; Camp_Phospho_Site 45- 48; Ck2_Phospho_Site 14-17, 56-59, 94-97, 262-265; Myristyl 207-212, 255-260; Pkc_Phospho_Site 76- 78, 94-96, 107-109, 122-124, 382-384; Tyr_Phospho_Site 55- 63, 193-201; |
| | N | 0 -o | 268-290,1.26; | Amidation 152-155; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|---|
| DEX0374_3. aa.9 | | | 237-246,1.216; 489-500,1.199; 44-73,1.187; 592- 604,1.181; 212- 233,1.172; 791- 799,1.172; 122- 146,1.171; 439- 471,1.17; 107- 114,1.165; 740- 774,1.16; 719- 729,1.16; 344- 358,1.159; 255- 265,1.137; 580- 586,1.135; 527- 551,1.132; 392- 408,1.127; 697- 712,1.12; 654- 661,1.12; 626- 651,1.117; 553- 561,1.117; 79- 90,1.113; 297- 317,1.107; 192- 198,1.104; 781- 788,1.094; 614- 623,1.093; 511- 520,1.092; 148- 155,1.082; 412- 421,1.08; 428- 436,1.079; 333- 339,1.074; 319- 325,1.071; 677- 686,1.066; 99- 105,1.066; 179- 185,1.057 | Asn_Glycosylation 80- 83, 232-235, 494-497, 512-515; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16- 19, 20-23, 24-27, 29- 32, 57-60, 96-99, 120- 123, 247-250, 268-271, 299-302, 318-321, 345- 348, 355-358, 476-479, 518-521, 556-559, 724- 727; Myristyl 66-71, 117-122, 177-182, 445- 450, 669-674, 717-722; Pkc_Phospho_Site 82- 84, 145-147, 181-183, 217-219, 242-244, 247- 249, 296-298, 299-301, 328-330, 355-357, 390- 392, 538-540, 556-558, 569-571, 584-586; Rgd 413-415, 456-458; Tyr_Phospho_Site 517- 525, 655-663; |
| DEX0374_3. aa.12 | N | 0 -o | 268-290,1.26; 791-817,1.253; 237-246,1.216; 489-500,1.199; 44-73,1.187; 592- 604,1.181; 212- 233,1.172; 122- 146,1.171; 439- 471,1.17; 107- 114,1.165; 740- 774,1.16; 719- 729,1.16; 344- 358,1.159; 255- 265,1.137; 580- 586,1.135; 527- 551,1.132; 392- 408,1.127; 697- 712,1.12; 654- 661,1.12; 626- 651,1.117; 553- 561,1.117; 79- | Amidation 152-155; Asn_Glycosylation 80- 83, 232-235, 494-497, 512-515; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16- 19, 20-23, 24-27, 29- 32, 57-60, 96-99, 120- 123, 247-250, 268-271, 299-302, 318-321, 345- 348, 355-358, 476-479, 518-521, 556-559, 724- 727; Myristyl 66-71, 117-122, 177-182, 445- 450, 669-674, 717-722; Pkc_Phospho_Site 82- 84, 145-147, 181-183, 217-219, 242-244, 247- 249, 296-298, 299-301, 328-330, 355-357, 390- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|--|--|
| | | | 90,1.113; 297-317,1.107; 192-198,1.104; 819-836,1.1; 781-788,1.094; 614-623,1.093; 511-520,1.092; 148-155,1.082; 412-421,1.08; 428-436,1.079; 333-339,1.074; 319-325,1.071; 677-686,1.066; 99-105,1.066; 179-185,1.057 | 392, 538-540, 556-558, 569-571, 584-586; Rgd 413-415, 456-458; Tyr_Phospho_Site 517-525, 655-663; |
| DEX0374_3. aa.13 | N | 0 -o | 268-290,1.26; 237-246,1.216; 489-500,1.199; 44-73,1.187; 592-604,1.181; 212-233,1.172; 122-146,1.171; 439-471,1.17; 107-114,1.165; 719-729,1.16; 344-358,1.159; 740-773,1.142; 255-265,1.137; 580-586,1.135; 527-551,1.132; 392-408,1.127; 697-712,1.12; 654-661,1.12; 626-651,1.117; 553-561,1.117; 79-90,1.113; 297-317,1.107; 192-198,1.104; 614-623,1.093; 511-520,1.092; 148-155,1.082; 412-421,1.08; 428-436,1.079; 333-339,1.074; 319-325,1.071; 677-686,1.066; 99-105,1.066; 179-185,1.057 | Amidation 152-155; Asn_Glycosylation 80-83, 232-235, 494-497, 512-515; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16-19, 20-23, 24-27, 29-32, 57-60, 96-99, 120-123, 247-250, 268-271, 299-302, 318-321, 345-348, 355-358, 476-479, 518-521, 556-559, 724-727, 768-771; Myristyl 66-71, 117-122, 177-182, 445-450, 669-674, 717-722; Pkc_Phospho_Site 82-84, 145-147, 181-183, 217-219, 242-244, 247-249, 296-298, 299-301, 328-330, 355-357, 390-392, 538-540, 556-558, 569-571, 584-586; Rgd 413-415, 456-458; Tyr_Phospho_Site 517-525, 655-663; |
| DEX0374_3. aa.14 | N | 0 -o | 268-290,1.26; 237-246,1.216; 44-73,1.187; 212-233,1.172; 122-146,1.171; 107-114,1.165; 344-358,1.159; 255- | Amidation 152-155; Asn_Glycosylation 80-83, 232-235; Camp_Phospho_Site 415-418; Ck2_Phospho_Site 16-19, 20-23, 24-27, 29- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|--|
| | | | 265,1.137; 79-90,1.113; 392-408,1.108; 297-317,1.107; 192-198,1.104; 148-155,1.082; 333-339,1.074; 319-325,1.071; 99-105,1.066; 179-185,1.057 | 32, 57-60, 96-99, 120-123, 247-250, 268-271, 299-302, 318-321, 345-348, 355-358; Myristyl 66-71, 117-122, 177-182; Pkc_Phospho_Site 82-84, 145-147, 181-183, 217-219, 242-244, 247-249, 296-298, 299-301, 328-330, 355-357, 390-392; |
| DEX0374_3. aa.15 | N | 0 -o | 268-290,1.26; 237-246,1.216; 44-73,1.187; 212-233,1.172; 122-146,1.171; 107-114,1.165; 255-265,1.137; 79-90,1.113; 297-336,1.107; 192-198,1.104; 148-155,1.082; 99-105,1.066; 179-185,1.057 | Amidation 152-155; Asn_Glycosylation 80-83, 232-235; Ck2_Phospho_Site 16-19, 20-23, 24-27, 29-32, 57-60, 96-99, 120-123, 247-250, 268-271, 299-302, 318-321, 324-327; Myristyl 66-71, 117-122, 177-182; Pkc_Phospho_Site 82-84, 145-147, 181-183, 217-219, 242-244, 247-249, 296-298, 299-301, 333-335; |
| DEX0374_3. aa.16 | N | 0 -o | 44-73,1.187; 122-146,1.171; 107-114,1.165; 79-90,1.113; 99-105,1.066 | Amidation 152-155; Asn_Glycosylation 80-83; Camp_Phospho_Site 154-157; Ck2_Phospho_Site 16-19, 20-23, 24-27, 29-32, 57-60, 96-99, 120-123; Myristyl 66-71, 117-122; Pkc_Phospho_Site 82-84, 145-147; |
| DEX0374_3. aa.19 | N | 0 -o | 193-215,1.26; 716-742,1.253; 162-171,1.216; 414-425,1.199; 29-39,1.197; 4-23,1.187; 517-529,1.181; 137-158,1.172; 47-71,1.171; 364-396,1.17; 665-699,1.16; 644-654,1.16; 269-283,1.159; 180-190,1.137; 505-511,1.135; 452-476,1.132; 757-765,1.132; 317-333,1.127; 622- | Amidation 77-80; Asn_Glycosylation 30-33, 157-160, 419-422, 437-440; Camp_Phospho_Site 432-435; Ck2_Phospho_Site 3-6, 45-48, 172-175, 193-196, 224-227, 243-246, 270-273, 280-283, 401-404, 443-446, 481-484, 649-652; Myristyl 16-21, 42-47, 102-107, 370-375, 594-599, 642-647; Pkc_Phospho_Site 32-34, 70-72, 106-108, 142-144, 167-169, 172-174, 221-223, 224-226, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|---|
| | | | 637,1.12; 579-586,1.12; 551-576,1.117; 478-486,1.117; 222-242,1.107; 117-123,1.104; 744-750,1.1; 706-713,1.094; 539-548,1.093; 436-445,1.092; 73-80,1.082; 337-346,1.08; 353-361,1.079; 258-264,1.074; 244-250,1.071; 602-611,1.066; 104-110,1.057 | 253-255, 280-282, 315-317, 463-465, 481-483, 494-496, 509-511, 769-771; Rgd 338-340, 381-383; Tyr_Phospho_Site 442-450, 580-588; |
| DEX0374_3. aa.22 | N | 0 -o | 268-290,1.26; 791-817,1.253; 237-246,1.216; 852-865,1.216; 489-500,1.199; 44-73,1.187; 592-604,1.181; 212-233,1.172; 122-146,1.171; 831-848,1.17; 439-471,1.17; 107-114,1.165; 740-774,1.16; 719-729,1.16; 344-358,1.159; 255-265,1.137; 580-586,1.135; 527-551,1.132; 392-408,1.127; 697-712,1.12; 654-661,1.12; 626-651,1.117; 553-561,1.117; 79-90,1.113; 297-317,1.107; 192-198,1.104; 819-827,1.1; 781-788,1.094; 614-623,1.093; 511-520,1.092; 148-155,1.082; 412-421,1.08; 428-436,1.079; 333-339,1.074; 319-325,1.071; 677-686,1.066; 99-105,1.066; 179-185,1.057 | Amidation 152-155; Asn_Glycosylation 80-83, 232-235, 494-497, 512-515; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16-19, 20-23, 24-27, 29-32, 57-60, 96-99, 120-123, 247-250, 268-271, 299-302, 318-321, 345-348, 355-358, 476-479, 518-521, 556-559, 724-727; Myristyl 66-71, 117-122, 177-182, 445-450, 669-674, 717-722; Pkc_Phospho_Site 82-84, 145-147, 181-183, 217-219, 242-244, 247-249, 296-298, 299-301, 328-330, 355-357, 390-392, 538-540, 556-558, 569-571, 584-586, 836-838, 869-871; Rgd 413-415, 456-458; Tyr_Phospho_Site 517-525, 655-663; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|---|
| DEX0374_3. aa.23 | N | 0 -o | 268-290,1.26; 237-246,1.216; 489-500,1.199; 44-73,1.187; 592- 604,1.181; 212- 233,1.172; 791- 802,1.172; 122- 146,1.171; 439- 471,1.17; 107- 114,1.165; 740- 774,1.16; 719- 729,1.16; 344- 358,1.159; 255- 265,1.137; 580- 586,1.135; 527- 551,1.132; 392- 408,1.127; 811- 823,1.125; 697- 712,1.12; 654- 661,1.12; 626- 651,1.117; 553- 561,1.117; 79- 90,1.113; 297- 317,1.107; 192- 198,1.104; 781- 788,1.094; 614- 623,1.093; 511- 520,1.092; 148- 155,1.082; 412- 421,1.08; 428- 436,1.079; 333- 339,1.074; 319- 325,1.071; 677- 686,1.066; 99- 105,1.066; 179- 185,1.057 | Amidation 152-155; Asn_Glycosylation 80- 83, 232-235, 494-497, 512-515, 812-815; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16- 19, 20-23, 24-27, 29- 32, 57-60, 96-99, 120- 123, 247-250, 268-271, 299-302, 318-321, 345- 348, 355-358, 476-479, 518-521, 556-559, 724- 727; Myristyl 66-71, 117-122, 177-182, 445- 450, 669-674, 717-722, 813-818; Pkc_Phospho_Site 82- 84, 145-147, 181-183, 217-219, 242-244, 247- 249, 296-298, 299-301, 328-330, 355-357, 390- 392, 538-540, 556-558, 569-571, 584-586, 814- 816; Rgd 413-415, 456-458; Tyr_Phospho_Site 517- 525, 655-663; |
| DEX0374_3. aa.24 | N | 0 -o | 268-290,1.26; 237-246,1.216; 489-500,1.199; 44-73,1.187; 212- 233,1.172; 122- 146,1.171; 439- 471,1.17; 107- 114,1.165; 344- 358,1.159; 255- 265,1.137; 392- 408,1.127; 79- 90,1.113; 297- 317,1.107; 192- 198,1.104; 148- 155,1.082; 412- 421,1.08; 428- 436,1.079; 333- 339,1.074; 319- 325,1.071; 99- | Amidation 152-155; Asn_Glycosylation 80- 83, 232-235, 494-497, 512-515; Camp_Phospho_Site 507-510; Ck2_Phospho_Site 16- 19, 20-23, 24-27, 29- 32, 57-60, 96-99, 120- 123, 247-250, 268-271, 299-302, 318-321, 345- 348, 355-358, 476-479, 518-521; Myristyl 66- 71, 117-122, 177-182, 445-450; Pkc_Phospho_Site 82- 84, 145-147, 181-183, 217-219, 242-244, 247- 249, 296-298, 299-301, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|---|
| | | | 105,1.066; 179-185,1.057 | 328-330, 355-357, 390-392; Rgd 413-415, 456-458; |
| DEX0374_3. aa.25 | N | 0 -o | 237-246,1.216; 44-73,1.187; 212-233,1.172; 122-146,1.171; 107-114,1.165; 255-266,1.165; 79-90,1.113; 192-198,1.104; 148-155,1.082; 99-105,1.066; 179-185,1.057 | Amidation 152-155; Asn_Glycosylation 80-83, 232-235; Ck2_Phospho_Site 16-19, 20-23, 24-27, 29-32, 57-60, 96-99, 120-123, 247-250; Myristyl 66-71, 117-122, 177-182; Pkc_Phospho_Site 82-84, 145-147, 181-183, 217-219, 242-244, 247-249; |
| DEX0374_6. aa.3 | N | 0 -o | 4-14,1.177; 18-53,1.164 | |
| DEX0374_6. aa.5 | Y | 0 -o | 157-173,1.165; 20-47,1.136; 50-61,1.125; 5-14,1.125; 108-115,1.106; 74-83,1.097; 175-182,1.093; 64-72,1.08; 221-228,1.079; 197-205,1.074; 141-147,1.043 | Amidation 244-247; Asn_Glycosylation 221-224, 236-239; Camp_Phospho_Site 125-128, 130-133; Ck2_Phospho_Site 99-102, 110-113, 133-136, 164-167, 210-213, 296-299, 313-316, 318-321; Myristyl 26-31, 46-51, 51-56, 143-148, 148-153; Pkc_Phospho_Site 89-91, 110-112, 128-130, 133-135, 217-219, 318-320; Tyr_Phospho_Site 219-225; |
| DEX0374_6. aa.10 | Y | 0 -o | 157-173,1.165; 20-47,1.136; 50-61,1.125; 5-14,1.125; 315-326,1.112; 367-375,1.109; 337-348,1.107; 108-115,1.106; 74-83,1.097; 350-359,1.093; 175-182,1.093; 379-391,1.09; 64-72,1.08; 221-228,1.079; 197-205,1.074; 141-147,1.043 | Amidation 244-247; Asn_Glycosylation 221-224, 236-239; Camp_Phospho_Site 125-128, 130-133; Ck2_Phospho_Site 99-102, 110-113, 133-136, 164-167, 210-213, 296-299, 313-316, 319-322, 331-334, 363-366, 388-391; Myristyl 26-31, 46-51, 51-56, 143-148, 148-153, 364-369, 394-399; Pkc_Phospho_Site 89-91, 110-112, 128-130, 133-135, 217-219; Tyr_Phospho_Site 219-225; |
| DEX0374_6. | Y | 0 -o | 157-173,1.165; 309-323,1.158; | Amidation 244-247; Asn_Glycosylation |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|--|---|
| aa.11 | | | 20-47,1.136; 50-61,1.125; 5-14,1.125; 108-115,1.106; 74-83,1.097; 175-182,1.093; 64-72,1.08; 221-228,1.079; 197-205,1.074; 141-147,1.043 | 221-224, 236-239; Camp_Phospho_Site 125-128, 130-133; Ck2_Phospho_Site 99-102, 110-113, 133-136, 164-167, 210-213, 296-299, 313-316; Myristyl 26-31, 46-51, 51-56, 143-148, 148-153; Pkc_Phospho_Site 89-91, 110-112, 128-130, 133-135, 217-219; Tyr_Phospho_Site 219-225; |
| DEX0374_6. aa.12 | Y | 0 -o | 157-173,1.165; 20-47,1.136; 50-61,1.125; 5-14,1.125; 108-115,1.106; 74-83,1.097; 175-182,1.093; 64-72,1.08; 141-147,1.043 | Camp_Phospho_Site 125-128, 130-133; Ck2_Phospho_Site 99-102, 110-113, 133-136, 164-167; Myristyl 26-31, 46-51, 51-56, 143-148, 148-153; Pkc_Phospho_Site 89-91, 110-112, 128-130, 133-135; |
| DEX0374_6. aa.15 | N | 0 -i | 79-101,1.237; 152-173,1.212; 41-61,1.159; 11-36,1.132; 117-125,1.085; 127-133,1.043 | Asn_Glycosylation 15-18, 118-121, 128-131; Ck2_Phospho_Site 78-81, 139-142, 151-154, 159-162; Myristyl 23-28, 108-113, 119-124; Pkc_Phospho_Site 14-16, 130-132, 136-138, 143-145, 174-176; |
| DEX0374_6. aa.16 | Y | 0 -o | 157-173,1.165; 20-47,1.136; 50-61,1.125; 5-14,1.125; 324-335,1.112; 376-384,1.109; 346-357,1.107; 407-426,1.107; 108-115,1.106; 74-83,1.097; 359-368,1.093; 175-182,1.093; 388-400,1.09; 64-72,1.08; 230-237,1.079; 428-437,1.072; 141-147,1.043 | Amidation 253-256; Asn_Glycosylation 230-233, 245-248; Camp_Phospho_Site 125-128, 130-133, 429-432; Ck2_Phospho_Site 99-102, 110-113, 133-136, 164-167, 219-222, 305-308, 322-325, 328-331, 340-343, 372-375, 397-400, 420-423; Myristyl 26-31, 46-51, 51-56, 143-148, 148-153, 373-378, 403-408; Pkc_Phospho_Site 89-91, 110-112, 128-130, 133-135, 210-212, 226-228, 432-434; Tyr_Phospho_Site 228-234; |
| DEX0374_6. | Y | 0 -o | 157-173,1.165; 20-47,1.136; 50- | Amidation 244-247; Asn_Glycosylation |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|--|--|
| aa.17 | | | 61,1.125; 5-14,1.125; 329-342,1.123; 315-326,1.112; 108-115,1.106; 74-83,1.097; 175-182,1.093; 64-72,1.08; 221-228,1.079; 197-205,1.074; 141-147,1.043 | 221-224, 236-239; Camp_Phospho_Site 125-128, 130-133; Ck2_Phospho_Site 99-102, 110-113, 133-136, 164-167, 210-213, 296-299, 313-316, 319-322, 331-334, 363-366; Myristyl 26-31, 46-51, 51-56, 143-148, 148-153, 380-385; Pkc_Phospho_Site 89-91, 110-112, 128-130, 133-135, 217-219, 363-365, 384-386; Tyr_Phospho_Site 219-225; |
| DEX0374_16 .aa.4 | N | 0 -o | 433-456,1.234; 375-384,1.204; 267-278,1.183; 57-76,1.183; 280-290,1.169; 126-134,1.168; 494-504,1.167; 410-424,1.166; 915-930,1.16; 149-168,1.155; 613-652,1.151; 464-481,1.15; 88-107,1.149; 110-121,1.142; 887-896,1.127; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 520-541,1.114; 938-952,1.112; 851-863,1.111; 244-254,1.11; 388-395,1.103; 697-708,1.1; 483-490,1.097; 555-566,1.097; 598-606,1.092; 834-840,1.09; 259-265,1.078; 870-881,1.076; 141-147,1.068; 810-816,1.064; 658-664,1.061; 799-806,1.058; 760-773,1.054; 26-39,1.047 | Amidation 461-464, 823-826; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465-468, 754-757, 940-943; Camp_Phospho_Site 760-763; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 617-620, 658-661, 676-679, 681-684, 700-703, 812-815, 840-843, 853-856, 887-890, 934-937, 942-945; Glycosaminoglycan 846-849; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 732-737, 733-738, 753-758, 762-767, 833-838, 837-842, 888-893; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 630-632, 640-642, 669-671, 721-723, 759-761, 950-952; Tyr_Phospho_Site 57-65; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|--|--|
| DEX0374_16 .aa.6 | N | 0 -o | 1237-1264,1.277; 1139-1177,1.255; 433-456,1.234; 1274-1298,1.224; 1777-1787,1.221; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1718-1736,1.193; 1181-1227,1.189; 1660-1668,1.185; 267-278,1.183; 57-76,1.183; 965- 983,1.175; 280- 290,1.169; 1532- 1551,1.169; 126- 134,1.168; 934- 950,1.168; 494- 504,1.167; 410- 424,1.166; 1553- 1566,1.165; 1020- 1037,1.164; 888- 899,1.164; 868- 883,1.16; 1350- 1371,1.156; 149- 168,1.155; 994- 1005,1.153; 464- 481,1.15; 88- 107,1.149; 110- 121,1.142; 1814- 1826,1.141; 1850- 1862,1.131; 1833- 1843,1.13; 840- 849,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1460- 1473,1.123; 4- 13,1.122; 1337- 1344,1.122; 189- 197,1.121; 1868- 1884,1.12; 1300- 1313,1.12; 1380- 1387,1.119; 1039- 1056,1.118; 1495- 1502,1.118; 1799- 1812,1.117; 520- 541,1.114; 1754- 1763,1.111; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42- 45, 201-204, 205-208, 217-220, 228-231, 230- 233, 241-244, 248-251, 314-317, 325-328, 330- 333, 509-512, 629-632, 634-637, 653-656, 765- 768, 793-796, 806-809, 840-843, 887-890, 933- 936; Glycosaminoglycan 799-802; Leucine_Zipper 947- 968; Myristyl 342- 347, 358-363, 362-367, 595-600, 598-603, 685- 690, 686-691, 706-711, 715-720, 786-791, 790- 795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213- 215, 230-232, 258-260, 259-261, 599-601, 622- 624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57- 65; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|--|
| | | | 1579,1.101; 650-661,1.1; 483-490,1.097; 555-566,1.097; 920-926,1.093; 598-606,1.092; 787-793,1.09; 1505-1513,1.081; 1478-1486,1.078; 259-265,1.078; 823-834,1.076; 1686-1694,1.069; 141-147,1.068; 763-769,1.064; 611-617,1.061; 1323-1330,1.059; 752-759,1.058; 1315-1321,1.055; 713-726,1.054; 26-39,1.047 | |
| DEX0374_16 .aa.7 | N | 0 -o | 805-832,1.277; 707-745,1.255; 4-24,1.234; 842-866,1.224; 1345-1355,1.221; 631-699,1.204; 976-992,1.197; 1174-1191,1.194; 1286-1304,1.193; 749-795,1.189; 1228-1236,1.185; 533-551,1.175; 1100-1119,1.169; 502-518,1.168; 62-72,1.167; 1121-1134,1.165; 588-605,1.164; 456-467,1.164; 436-451,1.16; 918-939,1.156; 562-573,1.153; 32-49,1.15; 1382-1394,1.141; 1418-1430,1.131; 1401-1411,1.13; 408-417,1.127; 1028-1041,1.123; 905-912,1.122; 1436-1452,1.12; 868-881,1.12; 948-955,1.119; 607-624,1.118; 1063-1070,1.118; 1367-1380,1.117; 88-109,1.114; 1322- | Amidation 29-32, 344-347; Asn_Glycosylation 33-36, 275-278, 535-538, 753-756, 987-990, 988-991; Camp_Phospho_Site 281-284; Ck2_Phospho_Site 77-80, 197-200, 202-205, 221-224, 333-336, 361-364, 374-377, 408-411, 455-458, 501-504, 704-707, 803-806, 838-841, 876-879, 893-896; Glycosaminoglycan 367-370; Leucine_Zipper 515-536; Myristyl 163-168, 166-171, 253-258, 254-259, 274-279, 283-288, 354-359, 358-363, 409-414, 474-479, 475-480, 627-632, 663-668, 722-727, 859-864; Pkc_Phospho_Site 167-169, 190-192, 242-244, 280-282, 562-564, 579-581, 704-706, 748-750, 752-754, 842-844, 845-847, 893-895, 905-907, 908-910; Prokar_Lipoprotein 984-994; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|--|
| | | | 1331,1.111; 372-384,1.111; 476-482,1.111; 1013-1021,1.104; 1141-1147,1.101; 218-229,1.1; 51-58,1.097; 123-134,1.097; 488-494,1.093; 166-174,1.092; 355-361,1.09; 1073-1081,1.081; 1046-1054,1.078; 391-402,1.076; 1254-1262,1.069; 331-337,1.064; 179-185,1.061; 891-898,1.059; 320-327,1.058; 883-889,1.055; 281-294,1.054 | |
| DEX0374_16 .aa.8 | N | 0 -o | 1121-1148,1.277; 1023-1061,1.255; 317-340,1.234; 1158-1182,1.224; 1661-1671,1.221; 947-1015,1.204; 259-268,1.204; 1292-1308,1.197; 1490-1507,1.194; 1602-1620,1.193; 1065-1111,1.189; 1544-1552,1.185; 151-162,1.183; 57-81,1.183; 849-867,1.175; 164-174,1.169; 1416-1435,1.169; 818-834,1.168; 378-388,1.167; 294-308,1.166; 1437-1450,1.165; 904-921,1.164; 772-783,1.164; 752-767,1.16; 1234-1255,1.156; 878-889,1.153; 348-365,1.15; 1698-1710,1.141; 1734-1746,1.131; 1717-1727,1.13; 724-733,1.127; 188-203,1.127; 41-48,1.127; 115-123,1.123; 1344- | Amidation 345-348, 660-663; Asn_Glycosylation 109-112, 207-210, 225-228, 235-238, 241-244, 250-253, 274-277, 349-352, 591-594, 851-854; Camp_Phospho_Site 597-600; Ck2_Phospho_Site 42-45, 85-88, 89-92, 101-104, 112-115, 114-117, 125-128, 132-135, 198-201, 209-212, 214-217, 393-396, 513-516, 518-521, 537-540, 649-652, 677-680, 690-693, 724-727, 771-774, 817-820; Glycosaminoglycan 683-686; Leucine_Zipper 831-852; Myristyl 226-231, 242-247, 246-251, 479-484, 482-487, 569-574, 570-575, 590-595, 599-604, 670-675, 674-679, 725-730, 790-795, 791-796, 943-948, 979-984; Pkc_Phospho_Site 97-99, 114-116, 142-144, 143-145, 483-485, 506-508, 558-560, 596-598, 878-880, 895-897; Tyr_Phospho_Site 57- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|--|
| | | | 1357,1.123; 4-13,1.122; 1221-1228,1.122; 1752-1768,1.12; 1184-1197,1.12; 1264-1271,1.119; 923-940,1.118; 1379-1386,1.118; 1683-1696,1.117; 404-425,1.114; 1638-1647,1.111; 688-700,1.111; 792-798,1.111; 128-138,1.11; 1329-1337,1.104; 272-279,1.103; 1457-1463,1.101; 534-545,1.1; 367-374,1.097; 439-450,1.097; 804-810,1.093; 482-490,1.092; 671-677,1.09; 1389-1397,1.081; 1362-1370,1.078; 143-149,1.078; 707-718,1.076; 1570-1578,1.069; 647-653,1.064; 495-501,1.061; 1207-1214,1.059; 636-643,1.058; 1199-1205,1.055; 597-610,1.054; 26-39,1.047 | 65; |
| DEX0374_16 .aa.9 | N | 0 -o | 753-780,1.277; 655-693,1.255; 790-814,1.224; 1293-1303,1.221; 579-647,1.204; 924-940,1.197; 1122-1139,1.194; 1234-1252,1.193; 697-743,1.189; 1176-1184,1.185; 130-151,1.179; 481-499,1.175; 1048-1067,1.169; 450-466,1.168; 1069-1082,1.165; 536-553,1.164; 404-415,1.164; 384-399,1.16; 866-887,1.156; 510-521,1.153; | Amidation 178-181, 292-295; Asn_Glycosylation 56-59, 223-226, 483-486, 701-704, 935-938, 936-939; Camp_Phospho_Site 12-15, 229-232; Ck2_Phospho_Site 68-71, 93-96, 124-127, 281-284, 309-312, 322-325, 356-359, 403-406, 449-452, 652-655, 751-754, 786-789, 824-827, 841-844; Glycosaminoglycan 315-318; Leucine_Zipper 463-484; Myristyl 48-53, 53-58, 109-114, 116-121, 129-134, 133-138, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| | | | 65-79,1.149; 1330-1342,1.141; 1366-1378,1.131; 1349-1359,1.13; 356-365,1.127; 976-989,1.123; 853-860,1.122; 1384-1400,1.12; 816-829,1.12; 896-903,1.119; 555-572,1.118; 1011-1018,1.118; 1315-1328,1.117; 9-16,1.115; 1270- 1279,1.111; 320- 332,1.111; 424- 430,1.111; 19- 26,1.106; 961- 969,1.104; 1089- 1095,1.101; 159- 172,1.093; 436- 442,1.093; 81- 89,1.092; 303- 309,1.09; 1021- 1029,1.081; 994- 1002,1.078; 339- 350,1.076; 1202- 1210,1.069; 279- 285,1.064; 839- 846,1.059; 268- 275,1.058; 831- 837,1.055; 229- 242,1.054 | 137-142, 201-206, 202- 207, 222-227, 231-236, 302-307, 306-311, 357- 362, 422-427, 423-428, 575-580, 611-616, 670- 675, 807-812, 953-958, 954-959, 955-960, 959- 964; Pkc_Phospho_Site 9-11, 19-21, 90-92, 93-95, 120-122, 190- 192, 228-230, 510-512, 527-529, 652-654, 696- 698, 700-702, 790-792, 793-795, 841-843, 853- 855, 856-858, 975-977; Prokar_Lipoprotein 932-942; |
| DEX0374_16 .aa.11 | N | 0 -o | 1237-1264,1.277; 1139-1177,1.255; 433-456,1.234; 1274-1298,1.224; 1799-1809,1.221; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1718-1736,1.193; 1181-1227,1.189; 1660-1668,1.185; 267-278,1.183; 57-76,1.183; 965- 983,1.175; 280- 290,1.169; 1532- 1551,1.169; 126- 134,1.168; 934- 950,1.168; 494- 504,1.167; 410- 424,1.166; 1553- 1566,1.165; 1020- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42- 45, 201-204, 205-208, 217-220, 228-231, 230- 233, 241-244, 248-251, 314-317, 325-328, 330- 333, 509-512, 629-632, 634-637, 653-656, 765- 768, 793-796, 806-809, 840-843, 887-890, 933- 936; Glycosaminoglycan 799-802; Leucine_Zipper 947- 968; Myristyl 342- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|------------|----------|-------|---|--|
| | | | 1037,1.164; 888- 899,1.164; 868- 883,1.16; 1350- 1371,1.156; 149- 168,1.155; 994- 1005,1.153; 1746- 1772,1.151; 464- 481,1.15; 88- 107,1.149; 110- 121,1.142; 1836- 1848,1.141; 1872- 1884,1.131; 1855- 1865,1.13; 840- 849,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1460- 1473,1.123; 4- 13,1.122; 1337- 1344,1.122; 189- 197,1.121; 1890- 1906,1.12; 1300- 1313,1.12; 1380- 1387,1.119; 1039- 1056,1.118; 1495- 1502,1.118; 1821- 1834,1.117; 520- 541,1.114; 1776- 1785,1.111; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- 1579,1.101; 650- 661,1.1; 483- 490,1.097; 555- 566,1.097; 920- 926,1.093; 598- 606,1.092; 787- 793,1.09; 1505- 1513,1.081; 1478- 1486,1.078; 259- 265,1.078; 823- 834,1.076; 1686- 1694,1.069; 141- 147,1.068; 763- 769,1.064; 611- 617,1.061; 1323- 1330,1.059; 752- 759,1.058; 1315- 1321,1.055; 713- 726,1.054; 26- 39,1.047 | 347, 358-363, 362-367, 595-600, 598-603, 685- 690, 686-691, 706-711, 715-720, 786-791, 790- 795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213- 215, 230-232, 258-260, 259-261, 599-601, 622- 624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57- 65; |
| | N | 0 -o | 1237-1264,1.277; | Amidation 461-464, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| DEX0374_16 .aa.16 | | | 1139-1177,1.255; 433-456,1.234; 1274-1298,1.224; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1181-1227,1.189; 1660-1668,1.185; 267-278,1.183; 57-76,1.183; 965- 983,1.175; 280- 290,1.169; 1532- 1551,1.169; 126- 134,1.168; 934- 950,1.168; 494- 504,1.167; 410- 424,1.166; 1553- 1566,1.165; 1020- 1037,1.164; 888- 899,1.164; 868- 883,1.16; 1350- 1371,1.156; 149- 168,1.155; 994- 1005,1.153; 464- 481,1.15; 88- 107,1.149; 110- 121,1.142; 1686- 1701,1.141; 840- 849,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1460- 1473,1.123; 4- 13,1.122; 1337- 1344,1.122; 189- 197,1.121; 1300- 1313,1.12; 1380- 1387,1.119; 1039- 1056,1.118; 1495- 1502,1.118; 520- 541,1.114; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- 1579,1.101; 650- 661,1.1; 483- 490,1.097; 555- 566,1.097; 920- 926,1.093; 598- 606,1.092; 787- 793,1.09; 1505- 1513,1.081; 1478- | 776-779; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42- 45, 201-204, 205-208, 217-220, 228-231, 230- 233, 241-244, 248-251, 314-317, 325-328, 330- 333, 509-512, 629-632, 634-637, 653-656, 765- 768, 793-796, 806-809, 840-843, 887-890, 933- 936; Glycosaminoglycan 799-802; Leucine_Zipper 947- 968; Myristyl 342- 347, 358-363, 362-367, 595-600, 598-603, 685- 690, 686-691, 706-711, 715-720, 786-791, 790- 795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213- 215, 230-232, 258-260, 259-261, 599-601, 622- 624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57- 65; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 1486,1.078; 259-265,1.078; 823-834,1.076; 141-147,1.068; 763-769,1.064; 611-617,1.061; 1323-1330,1.059; 752-759,1.058; 1315-1321,1.055; 713-726,1.054; 26-39,1.047 | |
| DEX0374_16 .aa.17 | N | 0 -o | 1139-1177,1.255; 433-456,1.234; 1063-1131,1.204; 375-384,1.204; 1181-1227,1.189; 267-278,1.183; 57-76,1.183; 965-983,1.175; 280-290,1.169; 126-134,1.168; 934-950,1.168; 494-504,1.167; 410-424,1.166; 1020-1037,1.164; 888-899,1.164; 868-883,1.16; 149-168,1.155; 994-1005,1.153; 464-481,1.15; 88-107,1.149; 110-121,1.142; 840-849,1.127; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 1039-1056,1.118; 520-541,1.114; 804-816,1.111; 908-914,1.111; 244-254,1.11; 388-395,1.103; 650-661,1.1; 483-490,1.097; 555-566,1.097; 920-926,1.093; 598-606,1.092; 787-793,1.09; 259-265,1.078; 823-834,1.076; 141-147,1.068; 763-769,1.064; 611-617,1.061; 752- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465-468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 629-632, 634-637, 653-656, 765-768, 793-796, 806-809, 840-843, 887-890, 933-936; Glycosaminoglycan 799-802; Leucine_Zipper 947-968; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 685-690, 686-691, 706-711, 715-720, 786-791, 790-795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 622-624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57-65; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|---|
| | | | 759,1.058; 713-726,1.054; 26-39,1.047 | |
| DEX0374_16 .aa.18 | N | 0 -o | 433-456,1.234; 375-384,1.204; 823-846,1.187; 267-278,1.183; 57-76,1.183; 280-290,1.169; 126-134,1.168; 494-504,1.167; 410-424,1.166; 149-168,1.155; 464-481,1.15; 88-107,1.149; 110-121,1.142; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 520-541,1.114; 804-816,1.111; 244-254,1.11; 388-395,1.103; 650-661,1.1; 483-490,1.097; 555-566,1.097; 598-606,1.092; 787-793,1.09; 259-265,1.078; 141-147,1.068; 763-769,1.064; 611-617,1.061; 752-759,1.058; 713-726,1.054; 26-39,1.047 | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465-468, 707-710; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 629-632, 634-637, 653-656, 765-768, 793-796, 806-809; Glycosaminoglycan 799-802; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 685-690, 686-691, 706-711, 715-720, 786-791, 790-795; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 622-624, 674-676, 712-714, 840-842; Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.20 | N | 0 -o | 259-281,1.186; 57-76,1.183; 126-134,1.168; 149-168,1.155; 88-107,1.149; 110-121,1.142; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 244-254,1.11; 141-147,1.068; 26-39,1.047 | Asn_Glycosylation 225-228; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261; Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.21 | N | 0 -o | 433-456,1.234; 375-384,1.204; 267-278,1.183; 57-76,1.183; 280-290,1.169; 126- | Amidation 461-464; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|---|
| | | | 134,1.168; 494-504,1.167; 410-424,1.166; 149-168,1.155; 464-481,1.15; 88-107,1.149; 110-121,1.142; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 520-541,1.114; 244-254,1.11; 388-395,1.103; 483-490,1.097; 555-566,1.097; 598-604,1.092; 259-265,1.078; 141-147,1.068; 26-39,1.047 | 468; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601; Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.22 | N | O -o | 1284-1311,1.277; 1186-1224,1.255; 433-456,1.234; 1321-1345,1.224; 1824-1834,1.221; 1110-1178,1.204; 375-384,1.204; 1455-1471,1.197; 1653-1670,1.194; 1765-1783,1.193; 1228-1274,1.189; 1707-1715,1.185; 267-278,1.183; 57-76,1.183; 1012-1030,1.175; 280-290,1.169; 1579-1598,1.169; 126-134,1.168; 981-997,1.168; 494-504,1.167; 410-424,1.166; 1600-1613,1.165; 1067-1084,1.164; 935-946,1.164; 915-930,1.16; 1397-1418,1.156; 149-168,1.155; 1041-1052,1.153; 613-652,1.151; 464-481,1.15; 88-107,1.149; 110-121,1.142; 1861-1873,1.141; 1897-1909,1.131; 1880- | Amidation 461-464, 823-826; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465-468, 754-757; Camp_Phospho_Site 760-763; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 617-620, 658-661, 676-679, 681-684, 700-703, 812-815, 840-843, 853-856, 887-890, 934-937, 980-983; Glycosaminoglycan 846-849; Leucine_Zipper 994-1015; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 732-737, 733-738, 753-758, 762-767, 833-838, 837-842, 888-893, 953-958, 954-959; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 630-632, 640-642, 669-671, 721-723, 759-761; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 1890,1.13; 887- 896,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1507- 1520,1.123; 4- 13,1.122; 1384- 1391,1.122; 189- 197,1.121; 1915- 1931,1.12; 1347- 1360,1.12; 1427- 1434,1.119; 1086- 1103,1.118; 1542- 1549,1.118; 1846- 1859,1.117; 520- 541,1.114; 1801- 1810,1.111; 851- 863,1.111; 955- 961,1.111; 244- 254,1.11; 1492- 1500,1.104; 388- 395,1.103; 1620- 1626,1.101; 697- 708,1.1; 483- 490,1.097; 555- 566,1.097; 967- 973,1.093; 598- 606,1.092; 834- 840,1.09; 1552- 1560,1.081; 1525- 1533,1.078; 259- 265,1.078; 870- 881,1.076; 1733- 1741,1.069; 141- 147,1.068; 810- 816,1.064; 658- 664,1.061; 1370- 1377,1.059; 799- 806,1.058; 1362- 1368,1.055; 760- 773,1.054; 26- 39,1.047 | Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.23 | N | 0 -o | 570-597,1.277; 472-510,1.255; 607-631,1.224; 1110-1120,1.221; 396-464,1.204; 741-757,1.197; 939-956,1.194; 1051-1069,1.193; 514-560,1.189; 993-1001,1.185; 298-316,1.175; 865-884,1.169; 267-283,1.168; | Amidation 109-112; Asn_Glycosylation 40-43, 300-303, 518-521, 752-755, 753-756; Camp_Phospho_Site 46-49, 968-971; Ck2_Phospho_Site 98-101, 126-129, 139-142, 173-176, 220-223, 266-269, 469-472, 568-571, 603-606, 641-644, 658-661, 822-825, 832-835, 841-844, 862-865, 880- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 886-899,1.165; 353-370,1.164; 221-232,1.164; 201-216,1.16; 683-704,1.156; 327-338,1.153; 1147-1159,1.141; 1183-1195,1.131; 1166-1176,1.13; 173-182,1.127; 793-806,1.123; 670-677,1.122; 1201-1217,1.12; 633-646,1.12; 713-720,1.119; 372-389,1.118; 828-835,1.118; 1132-1145,1.117; 1087-1096,1.111; 137-149,1.111; 241-247,1.111; 778-786,1.104; 906-912,1.101; 253-259,1.093; 120-126,1.09; 838-846,1.081; 811-819,1.078; 156-167,1.076; 1019-1027,1.069; 96-102,1.064; 656-663,1.059; 85-92,1.058; 648- 654,1.055; 46- 59,1.054 | 883; Glycosaminoglycan 132-135; Leucine_Zipper 280- 301; Myristyl 18-23, 19-24, 39-44, 48-53, 119-124, 123-128, 174- 179, 239-244, 240-245, 392-397, 428-433, 487- 492, 624-629, 770-775, 771-776, 772-777, 776- 781, 889-894; Pkc_Phospho_Site 3-5, 45-47, 327-329, 344- 346, 469-471, 513-515, 517-519, 607-609, 610- 612, 658-660, 670-672, 673-675, 792-794, 841- 843, 862-864, 903-905, 996-998; Prokar_Lipoprotein 749-759; |
| DEX0374_16 .aa.24 | N | 0 -o | 433-456,1.234; 1063-1123,1.204; 375-384,1.204; 267-278,1.183; 57-76,1.183; 965- 983,1.175; 280- 290,1.169; 126- 134,1.168; 934- 950,1.168; 494- 504,1.167; 410- 424,1.166; 1020- 1037,1.164; 888- 899,1.164; 868- 883,1.16; 149- 168,1.155; 994- 1005,1.153; 464- 481,1.15; 88- 107,1.149; 110- 121,1.142; 840- 849,1.127; 304- 319,1.127; 41- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42- 45, 201-204, 205-208, 217-220, 228-231, 230- 233, 241-244, 248-251, 314-317, 325-328, 330- 333, 509-512, 629-632, 634-637, 653-656, 765- 768, 793-796, 806-809, 840-843, 887-890, 933- 936; Glycosaminoglycan 799-802; Leucine_Zipper 947- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| | | | 48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 1039-1056,1.118; 520-541,1.114; 804-816,1.111; 908-914,1.111; 244-254,1.11; 388-395,1.103; 650-661,1.1; 483-490,1.097; 555-566,1.097; 920-926,1.093; 598-606,1.092; 787-793,1.09; 259-265,1.078; 823-834,1.076; 141-147,1.068; 763-769,1.064; 611-617,1.061; 752-759,1.058; 713-726,1.054; 26-39,1.047 | 968; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 685-690, 686-691, 706-711, 715-720, 786-791, 790-795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 622-624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.25 | N | 0 -o | 1237-1264,1.277; 1139-1177,1.255; 433-456,1.234; 1274-1298,1.224; 1777-1787,1.221; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1718-1736,1.193; 1181-1227,1.189; 1660-1668,1.185; 267-278,1.183; 57-76,1.183; 965-983,1.175; 280-290,1.169; 1532-1551,1.169; 126-134,1.168; 934-950,1.168; 494-504,1.167; 410-424,1.166; 1553-1566,1.165; 1020-1037,1.164; 888-899,1.164; 868-883,1.16; 1350-1371,1.156; 149-168,1.155; 994-1005,1.153; 464-481,1.15; 88-107,1.149; 110-121,1.142; 1814- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465-468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 629-632, 634-637, 653-656, 765-768, 793-796, 806-809, 840-843, 887-890, 933-936; Glycosaminoglycan 799-802; Leucine_Zipper 947-968; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 685-690, 686-691, 706-711, 715-720, 786-791, 790-795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 622- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|---|
| | | | 1826,1.141; 1850- 1862,1.131; 1833- 1843,1.13; 840- 849,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1460- 1473,1.123; 4- 13,1.122; 1337- 1344,1.122; 189- 197,1.121; 1868- 1890,1.12; 1300- 1313,1.12; 1380- 1387,1.119; 1039- 1056,1.118; 1495- 1502,1.118; 1799- 1812,1.117; 520- 541,1.114; 1754- 1763,1.111; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- 1579,1.101; 650- 661,1.1; 483- 490,1.097; 555- 566,1.097; 920- 926,1.093; 598- 606,1.092; 787- 793,1.09; 1505- 1513,1.081; 1478- 1486,1.078; 259- 265,1.078; 823- 834,1.076; 1686- 1694,1.069; 141- 147,1.068; 763- 769,1.064; 611- 617,1.061; 1323- 1330,1.059; 752- 759,1.058; 1315- 1321,1.055; 713- 726,1.054; 26- 39,1.047 | 624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57- 65; |
| DEX0374_16 .aa.26 | N | 0 -o | 1237-1264,1.277; 1139-1177,1.255; 433-456,1.234; 1274-1298,1.224; 1757-1767,1.221; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1181-1227,1.189; 1660-1668,1.185; | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42- 45, 201-204, 205-208, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|------------|----------|-------|---|---|
| | | | 267-278,1.183; 57-76,1.183; 965- 983,1.175; 280- 290,1.169; 1532- 1551,1.169; 126- 134,1.168; 934- 950,1.168; 494- 504,1.167; 410- 424,1.166; 1553- 1566,1.165; 1020- 1037,1.164; 888- 899,1.164; 868- 883,1.16; 1350- 1371,1.156; 149- 166,1.155; 994- 1005,1.153; 464- 481,1.15; 88- 107,1.149; 110- 121,1.142; 1794- 1806,1.141; 1830- 1842,1.131; 1813- 1823,1.13; 840- 849,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1460- 1473,1.123; 4- 13,1.122; 1337- 1344,1.122; 189- 197,1.121; 1848- 1864,1.12; 1300- 1313,1.12; 1380- 1387,1.119; 1039- 1056,1.118; 1495- 1502,1.118; 1779- 1792,1.117; 520- 541,1.114; 1734- 1743,1.111; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- 1579,1.101; 650- 661,1.1; 483- 490,1.097; 555- 566,1.097; 920- 926,1.093; 598- 606,1.092; 787- 793,1.09; 1718- 1730,1.089; 1505- 1513,1.081; 1478- 1486,1.078; 259- 265,1.078; 823- 834,1.076; 1686- | 217-220, 228-231, 230- 233, 241-244, 248-251, 314-317, 325-328, 330- 333, 509-512, 629-632, 634-637, 653-656, 765- 768, 793-796, 806-809, 840-843, 887-890, 933- 936; Glycosaminoglycan 799-802; Leucine_Zipper 947- 968; Myristyl 342- 347, 358-363, 362-367, 595-600, 598-603, 685- 690, 686-691, 706-711, 715-720, 786-791, 790- 795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213- 215, 230-232, 258-260, 259-261, 599-601, 622- 624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57- 65; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 1694,1.069; 141-147,1.068; 763-769,1.064; 611-617,1.061; 1323-1330,1.059; 752-759,1.058; 1315-1321,1.055; 713-726,1.054; 26-39,1.047 | |
| DEX0374_16 .aa.27 | N | 0 -o | 1237-1264,1.277; 1139-1177,1.255; 1850-1874,1.248; 433-456,1.234; 1274-1298,1.224; 1777-1787,1.221; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1718-1736,1.193; 1181-1227,1.189; 1660-1668,1.185; 267-278,1.183; 57-76,1.183; 965-983,1.175; 280-290,1.169; 1532-1551,1.169; 126-134,1.168; 934-950,1.168; 494-504,1.167; 410-424,1.166; 1553-1566,1.165; 1020-1037,1.164; 888-899,1.164; 868-883,1.16; 1350-1371,1.156; 149-168,1.155; 994-1005,1.153; 464-481,1.15; 88-107,1.149; 110-121,1.142; 1814-1826,1.141; 1833-1843,1.13; 840-849,1.127; 304-319,1.127; 41-48,1.127; 231-239,1.123; 1460-1473,1.123; 4-13,1.122; 1337-1344,1.122; 189-197,1.121; 1880-1902,1.12; 1300-1313,1.12; 1380-1387,1.119; 1039-1056,1.118; 1495- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393, 465-468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 629-632, 634-637, 653-656, 765-768, 793-796, 806-809, 840-843, 887-890, 933-936; Glycosaminoglycan 799-802; Leucine_Zipper 947-968; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 685-690, 686-691, 706-711, 715-720, 786-791, 790-795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 622-624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57-65; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| | | | 1502,1.118; 1799- 1812,1.117; 520- 541,1.114; 1754- 1763,1.111; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- 1579,1.101; 650- 661,1.1; 483- 490,1.097; 555- 566,1.097; 920- 926,1.093; 598- 606,1.092; 787- 793,1.09; 1505- 1513,1.081; 1478- 1486,1.078; 259- 265,1.078; 823- 834,1.076; 1686- 1694,1.069; 141- 147,1.068; 763- 769,1.064; 611- 617,1.061; 1323- 1330,1.059; 752- 759,1.058; 1315- 1321,1.055; 713- 726,1.054; 26- 39,1.047 | |
| DEX0374_16 .aa.28 | N | 0 -o | 1237-1264,1.277; 1139-1177,1.255; 433-456,1.234; 1274-1298,1.224; 1777-1787,1.221; 1063-1131,1.204; 375-384,1.204; 1408-1424,1.197; 1606-1623,1.194; 1718-1736,1.193; 1181-1227,1.189; 1660-1668,1.185; 267-278,1.183; 57-76,1.183; 965- 983,1.175; 1833- 1862,1.171; 280- 290,1.169; 1532- 1551,1.169; 126- 134,1.168; 934- 950,1.168; 494- 504,1.167; 410- 424,1.166; 1553- 1566,1.165; 1020- 1037,1.164; 888- 899,1.164; 868- 883,1.16; 1350- | Amidation 461-464, 776-779; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 707-710, 967-970; Camp_Phospho_Site 713-716; Ck2_Phospho_Site 42- 45, 201-204, 205-208, 217-220, 228-231, 230- 233, 241-244, 248-251, 314-317, 325-328, 330- 333, 509-512, 629-632, 634-637, 653-656, 765- 768, 793-796, 806-809, 840-843, 887-890, 933- 936; Glycosaminoglycan 799-802; Leucine_Zipper 947- 968; Myristyl 342- 347, 358-363, 362-367, 595-600, 598-603, 685- 690, 686-691, 706-711, 715-720, 786-791, 790- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| | | | 1371,1.156; 149- 168,1.155; 994- 1005,1.153; 464- 481,1.15; 88- 107,1.149; 110- 121,1.142; 1814- 1826,1.141; 840- 849,1.127; 304- 319,1.127; 41- 48,1.127; 231- 239,1.123; 1460- 1473,1.123; 4- 13,1.122; 1337- 1344,1.122; 189- 197,1.121; 1300- 1313,1.12; 1380- 1387,1.119; 1039- 1056,1.118; 1495- 1502,1.118; 1799- 1812,1.117; 520- 541,1.114; 1754- 1763,1.111; 804- 816,1.111; 908- 914,1.111; 244- 254,1.11; 1445- 1453,1.104; 388- 395,1.103; 1573- 1579,1.101; 650- 661,1.1; 483- 490,1.097; 555- 566,1.097; 920- 926,1.093; 598- 606,1.092; 787- 793,1.09; 1505- 1513,1.081; 1478- 1486,1.078; 259- 265,1.078; 823- 834,1.076; 1686- 1694,1.069; 141- 147,1.068; 1877- 1884,1.065; 763- 769,1.064; 611- 617,1.061; 1323- 1330,1.059; 752- 759,1.058; 1315- 1321,1.055; 713- 726,1.054; 26- 39,1.047 | 795, 841-846, 906-911, 907-912; Pkc_Phospho_Site 213- 215, 230-232, 258-260, 259-261, 599-601, 622- 624, 674-676, 712-714, 994-996; Tyr_Phospho_Site 57- 65; |
| DEX0374_16 .aa.29 | N | 0 -o | 433-456,1.234; 375-384,1.204; 267-278,1.183; 57-76,1.183; 704- 727,1.177; 280- 290,1.169; 126- 134,1.168; 494- | Amidation 461-464; Asn_Glycosylation 225-228, 323-326, 341- 344, 351-354, 357-360, 366-369, 390-393, 465- 468, 762-765, 766-769, 803-806, 832-835; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| | | | 504,1.167; 410-424,1.166; 149-168,1.155; 464-481,1.15; 88-107,1.149; 110-121,1.142; 661-671,1.132; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 520-541,1.114; 244-254,1.11; 769-776,1.108; 388-395,1.103; 650-659,1.1; 483-490,1.097; 852-858,1.097; 555-566,1.097; 598-606,1.092; 729-737,1.087; 783-790,1.082; 259-265,1.078; 673-681,1.075; 141-147,1.068; 743-750,1.067; 611-617,1.061; 26-39,1.047; 816-822,1.043 | Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333, 509-512, 629-632, 634-637, 653-656, 685-688, 708-711, 715-718, 732-735, 751-754, 764-767, 768-771, 795-798, 799-802, 862-865; Myristyl 342-347, 358-363, 362-367, 595-600, 598-603, 809-814; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261, 599-601, 622-624, 676-678, 751-753, 768-770, 843-845, 851-853; Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.30 | N | 0 -o | 375-384,1.204; 267-278,1.183; 57-76,1.183; 280-290,1.169; 126-134,1.168; 410-424,1.166; 149-168,1.155; 88-107,1.149; 110-121,1.142; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 244-254,1.11; 388-395,1.103; 259-265,1.078; 141-147,1.068; 26-39,1.047 | Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369, 390-393; Ck2_Phospho_Site 42-45, 201-204, 205-208, 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333; Myristyl 342-347, 358-363, 362-367; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261; Tyr_Phospho_Site 57-65; |
| DEX0374_16 .aa.31 | N | 0 -o | 267-278,1.183; 57-76,1.183; 280-290,1.169; 126-134,1.168; 389-410,1.166; 375-386,1.156; 149- | Asn_Glycosylation 225-228, 323-326, 341-344, 351-354, 357-360, 366-369; Ck2_Phospho_Site 42-45, 201-204, 205-208, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|--------------------|---|---|
| | | | 168,1.155; 88-107,1.149; 110-121,1.142; 304-319,1.127; 41-48,1.127; 231-239,1.123; 4-13,1.122; 189-197,1.121; 244-254,1.11; 259-265,1.078; 141-147,1.068; 26-39,1.047 | 217-220, 228-231, 230-233, 241-244, 248-251, 314-317, 325-328, 330-333; Myristyl 342-347, 358-363, 362-367; Pkc_Phospho_Site 213-215, 230-232, 258-260, 259-261; Tyr_Phospho_Site 57-65; |
| DEX0374_17 .aa.3 | N | 0 -o | 70-86,1.16; 8-27,1.141; 111-122,1.134; 43-49,1.133; 88-96,1.126; 55-64,1.096; 151-160,1.083; 133-139,1.078 | Asn_Glycosylation 58-61; Camp_Phospho_Site 40-43, 180-183; Ck2_Phospho_Site 43-46; Myristyl 56-61; Pkc_Phospho_Site 116-118, 145-147, 156-158, 163-165, 178-180, 183-185, 194-196; |
| DEX0374_17 .aa.4 | N | 0 -o | 13-28,1.173; 251-263,1.161; 143-159,1.16; 71-100,1.141; 184-195,1.134; 116-122,1.133; 31-48,1.132; 50-57,1.132; 224-244,1.13; 161-169,1.126; 128-137,1.096; 206-212,1.078 | Asn_Glycosylation 131-134; Camp_Phospho_Site 113-116; Ck2_Phospho_Site 69-72, 116-119, 251-254; Myristyl 9-14, 57-62, 66-71, 129-134; Pkc_Phospho_Site 189-191, 218-220, 229-231, 246-248; |
| DEX0374_17 .aa.5 | N | 0 -o | 201-241,1.167; 178-196,1.161; 70-86,1.16; 8-27,1.141; 111-122,1.134; 43-49,1.133; 151-171,1.13; 88-96,1.126; 55-64,1.096; 133-139,1.078 | Asn_Glycosylation 58-61; Camp_Phospho_Site 40-43; Ck2_Phospho_Site 43-46, 178-181, 201-204, 202-205, 247-250; Myristyl 56-61, 236-241; Pkc_Phospho_Site 116-118, 145-147, 156-158, 173-175; |
| DEX0374_17 .aa.6 | N | 1 - i65- 87o | 64-85,1.27; 47-62,1.143; 20-30,1.073 | Ck2_Phospho_Site 16-19; Pkc_Phospho_Site 21-23, 25-27; Prokar_Lipoprotein 79-89; |
| DEX0374_17 .aa.7 | N | 0 -o | 151-165,1.22; 70-86,1.16; 8-27,1.141; 111-122,1.134; 43-49,1.133; 88-96,1.126; 55-64,1.096; 133- | Asn_Glycosylation 58-61; Camp_Phospho_Site 40-43; Ck2_Phospho_Site 43-46, 165-168; Myristyl 56-61; Pkc_Phospho_Site 116- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|---|
| | | | 139,1.078 | 118, 145-147, 156-158; |
| DEX0374_17 .aa.9 | N | 0 -o | 95-107,1.161; 28-39,1.134; 68-88,1.13; 5-13,1.118; 50-56,1.078 | Ck2_Phospho_Site 5-8, 95-98; Pkc_Phospho_Site 5-7, 33-35, 62-64, 73-75, 90-92; |
| DEX0374_24 .aa.2 | N | 0 -o | 179-199,1.293; 333-362,1.171; 255-273,1.171; 217-230,1.16; 278-286,1.14; 24-40,1.122; 232-246,1.104; 104-117,1.102; 93-99,1.093; 304-314,1.092; 140-146,1.09; 291-297,1.078; 316-324,1.063; 129-135,1.043 | Amidation 152-155; Camp_Phospho_Site 104-107; Ck2_Phospho_Site 356-359; Glycosaminoglycan 156-159; Myristyl 54-59, 58-63, 64-69, 78-83, 79-84, 161-166, 165-170, 215-220, 347-352; Pkc_Phospho_Site 14-16, 75-77, 93-95, 129-131, 156-158, 212-214, 321-323; Prokar_Lipoprotein 222-232; |
| DEX0374_24 .aa.3 | Y | 0 -o | 4-23,1.293; 157-187,1.171; 79-97,1.171; 41-54,1.16; 102-110,1.14; 243-249,1.136; 56-70,1.104; 128-138,1.092; 115-121,1.078; 140-148,1.063; 280-286,1.021 | Amidation 231-234, 270-273, 332-335; Asn_Glycosylation 310-313; Camp_Phospho_Site 234-237; Ck2_Phospho_Site 180-183, 282-285, 294-297, 320-323, 328-331; Myristyl 39-44, 171-176, 196-201, 202-207, 265-270, 304-309; Pkc_Phospho_Site 36-38, 145-147, 279-281, 284-286, 312-314, 319-321, 320-322; Prokar_Lipoprotein 46-56; |
| DEX0374_27 .aa.2 | N | 0 -o | 4-25,1.182; 27-38,1.133; 43-51,1.132 | Pkc_Phospho_Site 13-15, 28-30; |
| DEX0374_35 .aa.2 | N | 0 -o | 15-57,1.21; 64-72,1.14; 118-138,1.081; 108-114,1.08; 81-90,1.055 | Glycosaminoglycan 75-78; Myristyl 107-112; Pkc_Phospho_Site 119-121; |
| DEX0374_39 .aa.3 | N | 0 -o | 28-40,1.189; 4-21,1.098 | Ck2_Phospho_Site 26-29; Pkc_Phospho_Site 14-16, 19-21; |
| DEX0374_43 .aa.3 | N | 0 -o | 26-72,1.133; 85-107,1.112 | Ck2_Phospho_Site 118-121; Myristyl 9-14, 72-77; Pkc_Phospho_Site 40-42, 44-46, 111-113; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|---|--|
| DEX0374_45 .aa.2 | Y | 0 -i | 101-129,1.21; 37-60,1.166; 91-99,1.111; 131-138,1.098; 10-21,1.085; 71-77,1.083 | Ck2_Phospho_Site 22-25, 84-87; Prokar_Lipoprotein 50-60; |
| DEX0374_53 .aa.3 | N | 0 -o | 611-626,1.248; 446-459,1.214; 952-962,1.204; 247-266,1.193; 639-649,1.16; 123-133,1.146; 666-685,1.141; 748-760,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 711-736,1.126; 474-483,1.124; 862-873,1.124; 408-423,1.123; 832-847,1.117; 236-242,1.112; 57-69,1.108; 509-517,1.105; 776-788,1.102; 158-165,1.101; 223-230,1.095; 807-819,1.091; 593-606,1.091; 191-199,1.088; 291-297,1.083; 269-276,1.079; 13-34,1.075; 141-153,1.069; 522-530,1.068; 82-88,1.064; 336-347,1.061; 548-554,1.061; 106-118,1.06; 91-99,1.056; 821-827,1.046; 431-439,1.037; 168-174,1.033; 561-567,1.032 | Amidation 195-198, 227-230, 304-307, 402-405; Asn_Glycosylation 769-772; Camp_Phospho_Site 306-309, 372-375, 528-531; Ck2_Phospho_Site 31-34, 135-138, 236-239, 321-324, 328-331, 363-366, 375-378, 383-386, 464-467, 477-480, 505-508, 573-576, 650-653, 739-742, 765-768, 796-799, 893-896, 894-897, 895-898, 899-902; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279-284, 356-361, 440-445, 549-554, 632-637, 890-895, 907-912, 946-951, 947-952, 949-954; Pkc_Phospho_Site 70-72, 80-82, 84-86, 135-137, 172-174, 195-197, 221-223, 301-303, 316-318, 328-330, 345-347, 371-373, 400-402, 468-470, 521-523, 541-543, 714-716, 729-731, 744-746, 851-853; Rgd 183-185, 954-956; |
| DEX0374_53 .aa.4 | N | 0 -o | 66-81,1.248; 94-104,1.16; 166-199,1.143; 15-38,1.142; 121-140,1.141; 48-61,1.091 | Ck2_Phospho_Site 17-20, 105-108, 202-205; Myristyl 34-39, 87-92; Pkc_Phospho_Site 45-47, 169-171, 184-186; |
| DEX0374_53 .aa.6 | N | 0 -o | 89-100,1.204; 4-11,1.124 | Ck2_Phospho_Site 30-33, 31-34, 32-35, 36-39; Myristyl 27-32, 44-49, 83-88, 84-89, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|-------|--|--|
| DEX0374_53 .aa.7 | N | 0 -o | 611-626,1.248; 446-459,1.214; 944-954,1.204; 247-266,1.193; 639-649,1.16; 123-133,1.146; 666-685,1.141; 748-760,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 711-736,1.126; 474-483,1.124; 854-865,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 509- 517,1.105; 776- 788,1.102; 158- 165,1.101; 223- 230,1.095; 807- 819,1.091; 593- 606,1.091; 191- 199,1.088; 291- 297,1.083; 269- 276,1.079; 13- 34,1.075; 141- 153,1.069; 522- 530,1.068; 82- 88,1.064; 336- 347,1.061; 548- 554,1.061; 106- 118,1.06; 91- 99,1.056; 821- 827,1.046; 431- 439,1.037; 168- 174,1.033; 561- 567,1.032 | 86-91; Rgd 91-93; Amidation 195-198, 227-230, 304-307, 402- 405; Asn_Glycosylation 769-772; Camp_Phospho_Site 306-309, 372-375, 528- 531; Ck2_Phospho_Site 31-34, 135-138, 236- 239, 321-324, 328-331, 363-366, 375-378, 383- 386, 464-467, 477-480, 505-508, 573-576, 650- 653, 739-742, 765-768, 796-799, 885-888, 886- 889, 887-890, 891-894; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279- 284, 356-361, 440-445, 549-554, 632-637, 835- 840, 882-887, 899-904, 938-943, 939-944, 941- 946; Pkc_Phospho_Site 70-72, 80-82, 84-86, 135-137, 172-174, 195- 197, 221-223, 301-303, 316-318, 328-330, 345- 347, 371-373, 400-402, 468-470, 521-523, 541- 543, 714-716, 729-731, 744-746, 843-845; Rgd 183-185, 946-948; |
| DEX0374_53 .aa.8 | N | 0 -o | 611-626,1.248; 446-459,1.214; 247-266,1.193; 639-649,1.16; 123-133,1.146; 666-685,1.141; 748-760,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 711-736,1.126; 474-483,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 509- 517,1.105; 776- | Amidation 195-198, 227-230, 304-307, 402- 405; Asn_Glycosylation 769-772; Camp_Phospho_Site 306-309, 372-375, 528- 531; Ck2_Phospho_Site 31-34, 135-138, 236- 239, 321-324, 328-331, 363-366, 375-378, 383- 386, 464-467, 477-480, 505-508, 573-576, 650- 653, 739-742, 765-768, 796-799; Glycosaminoglycan 221-224; Myristyl |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|---|
| | | | 788,1.102; 158-165,1.101; 223-230,1.095; 807-819,1.091; 593-606,1.091; 191-199,1.088; 291-297,1.083; 269-276,1.079; 13-34,1.075; 141-153,1.069; 522-530,1.068; 82-88,1.064; 336-347,1.061; 548-554,1.061; 106-118,1.06; 91-99,1.056; 821-827,1.046; 431-439,1.037; 168-174,1.033; 561-567,1.032 | 129-134, 142-147, 279-284, 356-361, 440-445, 549-554, 632-637; Pkc_Phospho_Site 70-72, 80-82, 84-86, 135-137, 172-174, 195-197, 221-223, 301-303, 316-318, 328-330, 345-347, 371-373, 400-402, 468-470, 521-523, 541-543, 714-716, 729-731, 744-746; Rgd 183-185; |
| DEX0374_53 .aa.10 | N | 0 -o | 123-138,1.248; 456-466,1.204; 151-161,1.16; 178-197,1.141; 260-272,1.139; 223-248,1.126; 366-377,1.124; 21-29,1.105; 288-300,1.102; 319-331,1.091; 105-118,1.091; 34-42,1.068; 60-66,1.061; 333-339,1.046; 73-79,1.032 | Asn_Glycosylation 281-284; Camp_Phospho_Site 40-43; Ck2_Phospho_Site 17-20, 85-88, 162-165, 251-254, 277-280, 308-311, 397-400, 398-401, 399-402, 403-406; Myristyl 61-66, 144-149, 347-352, 394-399, 411-416, 450-455, 451-456, 453-458; Pkc_Phospho_Site 33-35, 53-55, 226-228, 241-243, 256-258, 355-357; Rgd 458-460; |
| DEX0374_53 .aa.11 | N | 0 -o | 238-248,1.204; 42-54,1.139; 5-30,1.126; 148-159,1.124; 70-82,1.102; 101-113,1.091; 127-133,1.053; 115-121,1.046 | Asn_Glycosylation 63-66; Ck2_Phospho_Site 33-36, 59-62, 90-93, 179-182, 180-183, 181-184, 185-188; Myristyl 129-134, 176-181, 193-198, 232-237, 233-238, 235-240; Pkc_Phospho_Site 5-7, 23-25, 38-40, 137-139; Rgd 240-242; |
| DEX0374_53 .aa.12 | N | 0 -o | 611-626,1.248; 446-459,1.214; 247-266,1.193; 639-649,1.16; 123-133,1.146; 666-685,1.141; 387-395,1.131; 303-310,1.129; | Amidation 195-198, 227-230, 304-307, 402-405; Camp_Phospho_Site 306-309, 372-375, 528-531; Ck2_Phospho_Site 31-34, 135-138, 236-239, 321-324, 328-331, 363-366, 375-378, 383- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 180-187,1.128; 474-483,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 509- 517,1.105; 158- 165,1.101; 223- 230,1.095; 593- 606,1.091; 191- 199,1.088; 291- 297,1.083; 269- 276,1.079; 13- 34,1.075; 141- 153,1.069; 522- 530,1.068; 82- 88,1.064; 336- 347,1.061; 548- 554,1.061; 106- 118,1.06; 91- 99,1.056; 431- 439,1.037; 168- 174,1.033; 561- 567,1.032 | 386, 464-467, 477-480, 505-508, 573-576, 650- 653; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279- 284, 356-361, 440-445, 549-554, 632-637; Pkc_Phospho_Site 70- 72, 80-82, 84-86, 135- 137, 172-174, 195-197, 221-223, 301-303, 316- 318, 328-330, 345-347, 371-373, 400-402, 468- 470, 521-523, 541-543; Rgd 183-185; |
| DEX0374_53 .aa.13 | N | 0 -o | 611-626,1.248; 683-694,1.243; 446-459,1.214; 247-266,1.193; 639-649,1.16; 123-133,1.146; 674-681,1.132; 387-395,1.131; 303-310,1.129; 180-187,1.128; 474-483,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 509- 517,1.105; 158- 165,1.101; 223- 230,1.095; 593- 606,1.091; 191- 199,1.088; 291- 297,1.083; 269- 276,1.079; 13- 34,1.075; 141- 153,1.069; 522- 530,1.068; 82- 88,1.064; 336- 347,1.061; 548- 554,1.061; 106- 118,1.06; 91- 99,1.056; 431- 439,1.037; 168- 174,1.033; 561- 567,1.032 | Amidation 195-198, 227-230, 304-307, 402- 405; Camp_Phospho_Site 306-309, 372-375, 528- 531; Ck2_Phospho_Site 31-34, 135-138, 236- 239, 321-324, 328-331, 363-366, 375-378, 383- 386, 464-467, 477-480, 505-508, 573-576, 650- 653; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279- 284, 356-361, 440-445, 549-554, 632-637, 673- 678, 678-683, 685-690, 693-698; Pkc_Phospho_Site 70- 72, 80-82, 84-86, 135- 137, 172-174, 195-197, 221-223, 301-303, 316- 318, 328-330, 345-347, 371-373, 400-402, 468- 470, 521-523, 541-543; Rgd 183-185; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|---|
| DEX0374_53 .aa.14 | N | 0 -o | 238-248,1.204; 42-54,1.139; 5- 30,1.126; 148- 159,1.124; 70- 82,1.102; 101- 113,1.091; 127- 133,1.053; 115- 121,1.046 | Asn_Glycosylation 63- 66; Ck2_Phospho_Site 33-36, 59-62, 90-93, 179-182, 180-183, 181- 184, 185-188; Myristyl 129-134, 176-181, 193- 198, 232-237, 233-238, 235-240; Pkc_Phospho_Site 5-7, 23-25, 38-40, 137-139; Rgd 240-242; |
| DEX0374_53 .aa.15 | N | 0 -o | 446-459,1.214; 247-266,1.193; 123-133,1.146; 387-395,1.131; 303-310,1.129; 180-187,1.128; 474-483,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 548- 556,1.104; 158- 165,1.101; 533- 541,1.096; 223- 230,1.095; 191- 199,1.088; 291- 297,1.083; 517- 524,1.083; 269- 276,1.079; 13- 34,1.075; 141- 153,1.069; 82- 88,1.064; 336- 347,1.061; 106- 118,1.06; 91- 99,1.056; 431- 439,1.037; 168- 174,1.033 | Amidation 195-198, 227-230, 304-307, 402- 405; Camp_Phospho_Site 306-309, 372-375; Ck2_Phospho_Site 31- 34, 135-138, 236-239, 321-324, 328-331, 363- 366; 375-378, 383-386, 464-467, 477-480, 505- 508; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279- 284, 356-361, 440-445, 523-528, 547-552; Pkc_Phospho_Site 70- 72, 80-82, 84-86, 135- 137, 172-174, 195-197, 221-223, 301-303, 316- 318, 328-330, 345-347, 371-373, 400-402, 468- 470, 527-529; Rgd 183-185; |
| DEX0374_53 .aa.16 | N | 0 -o | 246-256,1.204; 42-54,1.139; 5- 30,1.126; 156- 167,1.124; 70- 82,1.102; 101- 113,1.091; 125- 132,1.057; 135- 141,1.053; 115- 121,1.046 | Asn_Glycosylation 63- 66; Ck2_Phospho_Site 33-36, 59-62, 90-93, 187-190, 188-191, 189- 192, 193-196; Myristyl 184-189, 201-206, 240- 245, 241-246, 243-248; Pkc_Phospho_Site 5-7, 23-25, 38-40, 145-147; Rgd 248-250; |
| DEX0374_53 .aa.17 | N | 0 -o | 21-29,1.105; 104- 118,1.091; 34- 42,1.068; 60- 66,1.061; 73- 79,1.032 | Camp_Phospho_Site 40- 43; Ck2_Phospho_Site 17-20, 85-88; Myristyl 61-66; Pkc_Phospho_Site 33- 35, 53-55; |
| DEX0374_53 | N | 0 -o | 66-81,1.248; 94- 104,1.16; 189- | Ck2_Phospho_Site 17- 20, 105-108, 125-128, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| .aa.18 | | | 222,1.143; 15-38,1.142; 141-149,1.136; 152-168,1.136; 122-139,1.11; 48-61,1.091 | 153-156; Myristyl 34-39, 87-92; Pkc_Phospho_Site 45-47, 127-129, 146-148, 207-209; |
| DEX0374_53 .aa.19 | N | 0 -o | 570-585,1.248; 903-913,1.204; 247-266,1.193; 598-608,1.16; 123-133,1.146; 625-644,1.141; 707-719,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 670-695,1.126; 813-824,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 468-476,1.105; 735-747,1.102; 158-165,1.101; 223-230,1.095; 766-778,1.091; 552-565,1.091; 191-199,1.088; 291-297,1.083; 269-276,1.079; 13-34,1.075; 141-153,1.069; 481-489,1.068; 82-88,1.064; 336-347,1.061; 507-513,1.061; 106-118,1.06; 91-99,1.056; 780-786,1.046; 431-439,1.037; 168-174,1.033; 520-526,1.032 | Amidation 195-198, 227-230, 304-307, 402-405; Asn_Glycosylation 728-731; Camp_Phospho_Site 306-309, 372-375, 487-490; Ck2_Phospho_Site 31-34, 135-138, 236-239, 321-324, 328-331, 363-366, 375-378, 383-386, 464-467, 532-535, 609-612, 698-701, 724-727, 755-758, 844-847, 845-848, 846-849, 850-853; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279-284, 356-361, 508-513, 591-596, 794-799, 841-846, 858-863, 897-902, 898-903, 900-905; Pkc_Phospho_Site 70-72, 80-82, 84-86, 135-137, 172-174, 195-197, 221-223, 301-303, 316-318, 328-330, 345-347, 371-373, 400-402, 480-482, 500-502, 673-675, 688-690, 703-705, 802-804; Rgd 183-185, 905-907; |
| DEX0374_53 .aa.20 | N | 0 -o | 611-626,1.248; 446-459,1.214; 247-266,1.193; 639-649,1.16; 123-133,1.146; 666-685,1.141; 748-760,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 711-736,1.126; 474-483,1.124; 408-423,1.123; | Amidation 195-198, 227-230, 304-307, 402-405; Asn_Glycosylation 769-772; Camp_Phospho_Site 306-309, 372-375, 528-531; Ck2_Phospho_Site 31-34, 135-138, 236-239, 321-324, 328-331, 363-366, 375-378, 383-386, 464-467, 477-480, 505-508, 573-576, 650-653, 739-742, 765-768, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 236-242,1.112; 57-69,1.108; 509- 517,1.105; 776- 788,1.102; 158- 165,1.101; 223- 230,1.095; 807- 819,1.091; 593- 606,1.091; 191- 199,1.088; 291- 297,1.083; 269- 276,1.079; 13- 34,1.075; 141- 153,1.069; 522- 530,1.068; 82- 88,1.064; 336- 347,1.061; 548- 554,1.061; 106- 118,1.06; 91- 99,1.056; 834- 842,1.053; 821- 827,1.046; 431- 439,1.037; 168- 174,1.033; 561- 567,1.032 | 796-799; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279- 284, 356-361, 440-445, 549-554, 632-637, 835- 840; Pkc_Phospho_Site 70-72, 80-82, 84-86, 135-137, 172-174, 195- 197, 221-223, 301-303, 316-318, 328-330, 345- 347, 371-373, 400-402, 468-470, 521-523, 541- 543, 714-716, 729-731, 744-746, 843-845; Rgd 183-185; |
| DEX0374_53 .aa.21 | N | 0 -o | 611-626,1.248; 446-459,1.214; 247-266,1.193; 800-814,1.187; 639-649,1.16; 123-133,1.146; 666-685,1.141; 748-760,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 711-736,1.126; 474-483,1.124; 408-423,1.123; 236-242,1.112; 57-69,1.108; 907- 922,1.107; 509- 517,1.105; 776- 788,1.102; 158- 165,1.101; 223- 230,1.095; 593- 606,1.091; 191- 199,1.088; 291- 297,1.083; 269- 276,1.079; 13- 34,1.075; 141- 153,1.069; 522- 530,1.068; 82- 88,1.064; 885- 893,1.063; 336- 347,1.061; 548- | Amidation 195-198, 227-230, 304-307, 402- 405, 845-848, 877-880; Asn_Glycosylation 769-772; Camp_Phospho_Site 306-309, 372-375, 528- 531, 861-864, 862-865; Ck2_Phospho_Site 31- 34, 135-138, 236-239, 321-324, 328-331, 363- 366, 375-378, 383-386, 464-467, 477-480, 505- 508, 573-576, 650-653, 739-742, 765-768, 796- 799; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279- 284, 356-361, 440-445, 549-554, 632-637, 845- 850, 849-854, 874-879, 902-907; Pkc_Phospho_Site 70- 72, 80-82, 84-86, 135- 137, 172-174, 195-197, 221-223, 301-303, 316- 318, 328-330, 345-347, 371-373, 400-402, 468- 470, 521-523, 541-543, 714-716, 729-731, 744- 746, 813-815, 834-836, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|--|
| | | | 554,1.061; 106-118,1.06; 91-99,1.056; 431-439,1.037; 168-174,1.033; 561-567,1.032 | 841-843, 857-859, 860-862, 877-879; Rgd 183-185; |
| DEX0374_53 .aa.22 | N | 0 -o | 611-626,1.248; 446-459,1.214; 997-1007,1.204; 247-266,1.193; 687-705,1.188; 639-649,1.16; 730-744,1.153; 123-133,1.146; 666-685,1.141; 801-813,1.139; 387-395,1.131; 303-310,1.129; 180-187,1.128; 764-789,1.126; 474-483,1.124; 907-918,1.124; 408-423,1.123; 236-242,1.112; 709-719,1.11; 57-69,1.108; 509-517,1.105; 829-841,1.102; 158-165,1.101; 223-230,1.095; 860-872,1.091; 593-606,1.091; 191-199,1.088; 291-297,1.083; 269-276,1.079; 13-34,1.075; 141-153,1.069; 522-530,1.068; 82-88,1.064; 336-347,1.061; 548-554,1.061; 106-118,1.06; 91-99,1.056; 874-880,1.046; 431-439,1.037; 168-174,1.033; 561-567,1.032 | Amidation 195-198, 227-230, 304-307, 402-405; Asn_Glycosylation 822-825; Camp_Phospho_Site 306-309, 372-375, 528-531; Ck2_Phospho_Site 31-34, 135-138, 236-239, 321-324, 328-331, 363-366, 375-378, 383-386, 464-467, 477-480, 505-508, 573-576, 650-653, 792-795, 818-821, 849-852, 938-941, 939-942, 940-943, 944-947; Glycosaminoglycan 221-224; Myristyl 129-134, 142-147, 279-284, 356-361, 440-445, 549-554, 632-637, 718-723, 888-893, 935-940, 952-957, 991-996, 992-997, 994-999; Pkc_Phospho_Site 70-72, 80-82, 84-86, 135-137, 172-174, 195-197, 221-223, 301-303, 316-318, 328-330, 345-347, 371-373, 400-402, 468-470, 521-523, 541-543, 767-769, 782-784, 797-799, 896-898; Rgd 183-185, 999-1001; Prokar_Lipoprotein 711-721; |
| DEX0374_53 .aa.23 | N | 0 -o | 310-320,1.204; 4-18,1.157; 43-57,1.153; 114-126,1.139; 77-102,1.126; 220-231,1.124; 22-32,1.11; 142-154,1.102; 173- | Asn_Glycosylation 135-138; Ck2_Phospho_Site 105-108, 131-134, 162-165, 251-254, 252-255, 253-256, 257-260; Myristyl 31-36, 201-206, 248-253, 265-270, 304-309, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|--|
| | | | 185,1.091; 187-193,1.046 | 305-310, 307-312; Pkc_Phospho_Site 80-82, 95-97, 110-112, 209-211; Rgd 312-314; Prokar_Lipoprotein 24-34; |
| DEX0374_53 .aa.25 | N | 0 -o | 63-74,1.124; 208-220,1.111; 160-166,1.11; 115-126,1.109; 254-266,1.091; 145-155,1.087; 128-136,1.083; 39-50,1.074; 6-12,1.062; 245-252,1.02 | Amidation 172-175; Camp_Phospho_Site 210-213; Ck2_Phospho_Site 94-97, 95-98, 96-99, 100-103, 161-164, 190-193, 194-197, 257-260; Myristyl 13-18, 91-96, 108-113, 198-203, 201-206, 205-210, 239-244, 252-257; Pkc_Phospho_Site 26-28, 172-174, 209-211, 261-263; |
| DEX0374_53 .aa.26 | Y | 0 -o | 5-17,1.221; 25-46,1.165; 119-130,1.124; 265-276,1.111; 216-222,1.11; 172-182,1.109; 88-95,1.093; 64-77,1.091; 310-322,1.091; 202-211,1.087; 186-192,1.083; 98-104,1.053 | Amidation 228-231; Camp_Phospho_Site 266-269; Ck2_Phospho_Site 53-56, 150-153, 151-154, 152-155, 156-159, 217-220, 246-249, 250-253, 313-316; Myristyl 147-152, 164-169, 254-259, 257-262, 261-266, 295-300, 308-313; Pkc_Phospho_Site 108-110, 228-230, 265-267, 317-319; |
| DEX0374_56 .aa.3 | N | 0 -o | 33-79,1.271; 4-21,1.165; 97-106,1.14 | Asn_Glycosylation 115-118; Ck2_Phospho_Site 24-27, 48-51, 116-119; Myristyl 33-38, 93-98, 100-105; Pkc_Phospho_Site 29-31, 34-36, 76-78; |
| DEX0374_56 .aa.4 | N | 0 -o | 105-115,1.217; 501-510,1.204; 161-171,1.187; 336-345,1.175; 133-143,1.158; 349-374,1.156; 473-480,1.147; 308-315,1.147; 188-212,1.125; 376-398,1.125; 513-533,1.115; 24-39,1.115; 252-258,1.108; 12- | Zinc_Finger_C2h2 114-134, 142-162, 169-190, 170-190, 198-218, 288-308, 316-336, 344-364, 373-393, 453-473, 481-501, 509-529; Amidation 117-120, 319-322, 484-487; Asn_Glycosylation 13-16, 328-331, 335-338, 493-496, 500-503; Camp_Phospho_Site 119-122, 175-178, 321- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|--------------------|---|---|
| | | | 18,1.102; 280-286,1.101; 445-451,1.101; 174-183,1.096; 93-101,1.095; 234-242,1.079; 222-231,1.078; 406-415,1.076; 458-467,1.072; 119-127,1.068; 265-272,1.055; 296-302,1.046; 45-54,1.035 | 324, 486-489; Ck2_Phospho_Site 83-86, 106-109, 197-200, 275-278, 536-539; Glycosaminoglycan 107-110; Myristyl 7-12, 12-17, 14-19, 70-75, 224-229, 259-264, 266-271, 269-274, 429-434; Pkc_Phospho_Site 76-78, 126-128, 150-152, 178-180, 324-326, 379-381, 424-426, 489-491, 517-519, 536-538; |
| DEX0374_56 .aa.9 | N | 1 - o44- 63i | 46-65,1.197; 24-39,1.115; 12-18,1.102 | Asn_Glycosylation 13-16; Myristyl 7-12, 12-17, 14-19; Pkc_Phospho_Site 62-64; Prokar_Lipoprotein 50-60; |
| DEX0374_56 .aa.12 | N | 0 -o | 514-523,1.204; 174-184,1.187; 113-123,1.182; 349-358,1.175; 35-62,1.166; 146-156,1.158; 362-387,1.156; 486-493,1.147; 321-328,1.147; 74-80,1.128; 201-225,1.125; 389-411,1.125; 22-30,1.12; 526-546,1.115; 265-271,1.108; 293-299,1.101; 458-464,1.101; 187-196,1.096; 88-95,1.092; 247-255,1.079; 235-244,1.078; 419-428,1.076; 471-480,1.072; 132-140,1.068; 278-285,1.055; 309-315,1.046 | Zinc_Finger_C2h2 155-175, 182-203, 183-203, 211-231, 301-321, 329-349, 357-377, 386-406, 466-486, 494-514, 522-542; Atp_Gtp_A 87-94; Amidation 130-133, 332-335, 497-500; Asn_Glycosylation 79-82, 341-344, 348-351, 506-509, 513-516; Camp_Phospho_Site 132-135, 188-191, 334-337, 499-502; Ck2_Phospho_Site 73-76, 210-213, 288-291, 549-552; Myristyl 68-73, 237-242, 272-277, 279-284, 282-287, 442-447; Pkc_Phospho_Site 103-105, 139-141, 163-165, 191-193, 337-339, 392-394, 437-439, 502-504, 530-532, 549-551; |
| DEX0374_56 .aa.13 | N | 0 -o | 105-115,1.217; 161-171,1.187; 133-143,1.158; 174-194,1.115; 24-39,1.115; 12-18,1.102; 93-101,1.095; 119-127,1.068; 45-54,1.035 | Zinc_Finger_C2h2 114-134, 142-162, 169-190, 170-190; Amidation 117-120; Asn_Glycosylation 13-16; Camp_Phospho_Site 119-122, 175-178; Ck2_Phospho_Site 83-86, 106-109, 197-200; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|---------------------|----------|---|---|--|
| | | | | Glycosaminoglycan 107-110; Myristyl 7-12, 12-17, 14-19, 70-75; Pkc_Phospho_Site 76-78, 126-128, 150-152, 178-180, 197-199; |
| DEX0374_60 .aa.3 | N | 0 -o | 35-61,1.222; 64-73,1.16; 101-112,1.122; 5-12,1.072 | Asn_Glycosylation 106-109; Ck2_Phospho_Site 96-99; Myristyl 3-8, 46-51; Tyr_Phospho_Site 36-44; |
| DEX0374_70 .aa.2 | N | 0 -o | 10-16,1.094; 32-49,1.092 | Ck2_Phospho_Site 60-63; Myristyl 30-35, 33-38; |
| DEX0374_70 .aa.3 | N | 0 -i | 10-16,1.094; 32-49,1.092 | Myristyl 30-35, 33-38; |
| DEX0374_73 .aa.3 | Y | 7 - o20- 42i55- 77o81- 103i12 0- 142o15 2- 171i17 8- 200o22 4-246i | 4-253,1.334; 282-318,1.14; 263-270,1.114 | Leucine_Zipper 129-150; Myristyl 12-17, 237-242, 278-283; Pkc_Phospho_Site 15-17, 172-174, 175-177, 299-301; Prokar_Lipoprotein 64-74, 108-118, 110-120, 228-238; |
| DEX0374_73 .aa.8 | N | 0 -o | 83-146,1.214; 5-77,1.186 | Ck2_Phospho_Site 30-33, 77-80; Leucine_Zipper 69-90; Myristyl 110-115; Pkc_Phospho_Site 143-145; |
| DEX0374_73 .aa.9 | N | 0 -o | 79-87,1.201; 180-214,1.193; 273-282,1.175; 4-27,1.173; 295-314,1.169; 56-76,1.168; 321-329,1.152; 237-245,1.151; 338-345,1.148; 140-155,1.147; 371-384,1.123; 89-104,1.121; 34-40,1.115; 167-176,1.112; 116-126,1.106; 255-261,1.098; 128-134,1.092; 361-368,1.084; 351-357,1.076 | Asn_Glycosylation 35-38, 258-261, 343-346; Camp_Phospho_Site 220-223; Ck2_Phospho_Site 37-40, 138-141; Glycosaminoglycan 276-279; Myristyl 68-73, 174-179, 186-191, 209-214, 224-229, 272-277; Pkc_Phospho_Site 47-49, 153-155, 178-180, 218-220, 251-253, 289-291, 372-374; |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|----------------------|--|---|
| DEX0374_73 .aa.11 | N | 0 -o | 10-16,1.024 | Pkc_Phospho_Site 19-21, 25-27; |
| DEX0374_73 .aa.12 | N | 0 -o | 79-87,1.201; 166-175,1.188; 4-27,1.173; 56-76,1.168; 89-104,1.121; 34-40,1.115; 116-126,1.106; 128-139,1.098; 150-156,1.067 | Asn_Glycosylation 35-38; Ck2_Phospho_Site 37-40; Myristyl 68-73, 148-153; Pkc_Phospho_Site 47-49; |
| DEX0374_80 .aa.2 | N | 1 - o704- 726i | 607-619,1.309; 219-253,1.257; 703-725,1.239; 153-172,1.217; 107-150,1.215; 257-265,1.202; 9-35,1.178; 649-675,1.167; 621-640,1.166; 501-517,1.16; 363-375,1.157; 269-295,1.153; 308-315,1.147; 678-690,1.139; 474-481,1.128; 593-605,1.115; 344-350,1.111; 297-303,1.101; 455-465,1.099; 544-555,1.098; 421-430,1.091; 192-213,1.086; 582-588,1.076; 97-103,1.074; 532-538,1.073; 488-494,1.049; 178-184,1.033 | Amidation 321-324; Asn_Glycosylation 82-85, 154-157, 524-527, 545-548; Camp_Phospho_Site 323-326, 337-340; Ck2_Phospho_Site 184-187, 201-204, 217-220, 340-343, 345-348, 398-401, 446-449, 529-532, 602-605, 670-673; Glycosaminoglycan 328-331; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60, 67-72, 80-85, 213-218, 331-336, 442-447, 489-494, 614-619, 662-667; Pkc_Phospho_Site 84-86, 217-219, 406-408, 446-448, 478-480, 573-575; Tyr_Phospho_Site 300-306; Pts_Hpr_Ser 474-489; |
| DEX0374_80 .aa.5 | N | 0 -o | 565-577,1.309; 177-211,1.257; 107-151,1.215; 215-223,1.202; 607-651,1.191; 9-35,1.178; 579-598,1.166; 459-475,1.16; 321-333,1.157; 227-253,1.153; 266-273,1.147; 432-439,1.128; 551-563,1.115; 302-308,1.111; 255-261,1.101; 413-423,1.099; 502- | Amidation 279-282; Asn_Glycosylation 82-85, 482-485, 503-506; Camp_Phospho_Site 281-284, 295-298; Ck2_Phospho_Site 175-178, 298-301, 303-306, 356-359, 404-407, 487-490, 560-563; Glycosaminoglycan 286-289; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60, 67-72, 80-85, 171-176, 289-294, 400-405, 447-452, 572- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|--|---|
| | | | 513,1.098; 379-388,1.091; 540-546,1.076; 97-103,1.074; 490-496,1.073; 157-171,1.069; 446-452,1.049 | 577; Pkc_Phospho_Site 84-86, 175-177, 364-366, 404-406, 436-438, 531-533; Tyr_Phospho_Site 258-264; Pts_Hpr_Ser 432-447; |
| DEX0374_80 .aa.7 | N | 0 -o | 607-619,1.309; 219-253,1.257; 153-172,1.217; 107-150,1.215; 257-265,1.202; 649-693,1.191; 9-35,1.178; 621-640,1.166; 501-517,1.16; 363-375,1.157; 269-295,1.153; 308-315,1.147; 474-481,1.128; 593-605,1.115; 344-350,1.111; 297-303,1.101; 455-465,1.099; 544-555,1.098; 421-430,1.091; 192-213,1.086; 582-588,1.076; 97-103,1.074; 532-538,1.073; 488-494,1.049; 178-184,1.033 | Amidation 321-324; Asn_Glycosylation 82-85, 154-157, 524-527, 545-548; Camp_Phospho_Site 323-326, 337-340; Ck2_Phospho_Site 184-187, 201-204, 217-220, 340-343, 345-348, 398-401, 446-449, 529-532, 602-605; Glycosaminoglycan 328-331; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60, 67-72, 80-85, 213-218, 331-336, 442-447, 489-494, 614-619; Pkc_Phospho_Site 84-86, 217-219, 406-408, 446-448, 478-480, 573-575; Tyr_Phospho_Site 300-306; Pts_Hpr_Ser 474-489; |
| DEX0374_80 .aa.8 | N | 0 -i | 11-55,1.191 | |
| DEX0374_80 .aa.10 | Y | 0 -o | 4-22,1.275; 30-62,1.191 | Ck2_Phospho_Site 32-35; Pkc_Phospho_Site 27-29; |
| DEX0374_80 .aa.13 | N | 0 -o | 219-253,1.257; 153-172,1.217; 107-150,1.215; 257-265,1.202; 9-35,1.178; 501-517,1.16; 363-375,1.157; 269-295,1.153; 308-315,1.147; 474-481,1.128; 344-350,1.111; 297-303,1.101; 455-465,1.099; 525-532,1.096; 421-430,1.091; 192-213,1.086; 97-103,1.074; 488- | Amidation 321-324; Asn_Glycosylation 82-85, 154-157, 524-527; Camp_Phospho_Site 323-326, 337-340; Ck2_Phospho_Site 184-187, 201-204, 217-220, 340-343, 345-348, 398-401, 446-449, 529-532; Glycosaminoglycan 328-331; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60, 67-72, 80-85, 213-218, 331-336, 442-447, 489-494; Pkc_Phospho_Site 84- |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|-------|---|---|
| | | | 494,1.049; 178-184,1.033 | 86, 217-219, 406-408, 446-448, 478-480; Tyr_Phospho_Site 300-306; Pts_Hpr_Ser 474-489; |
| DEX0374_80 .aa.14 | N | 0 -o | 219-253,1.257; 153-172,1.217; 107-150,1.215; 257-265,1.202; 9-35,1.178; 269-295,1.153; 308-314,1.147; 297-303,1.101; 192-213,1.086; 97-103,1.074; 178-184,1.033 | Asn_Glycosylation 82-85, 154-157; Ck2_Phospho_Site 184-187, 201-204, 217-220; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60, 67-72, 80-85, 213-218; Pkc_Phospho_Site 84-86, 217-219; Tyr_Phospho_Site 300-306; |
| DEX0374_80 .aa.16 | N | 0 -o | 90-102,1.309; 132-176,1.191; 104-123,1.166; 76-88,1.115; 27-38,1.098; 65-71,1.076; 15-21,1.073 | Asn_Glycosylation 28-31; Ck2_Phospho_Site 12-15, 85-88; Myristyl 97-102; Pkc_Phospho_Site 56-58; |
| DEX0374_80 .aa.18 | N | 0 -o | 9-35,1.178; 57-74,1.161 | Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60; Pkc_Phospho_Site 76-78; |
| DEX0374_80 .aa.19 | N | 0 -o | 219-253,1.257; 153-172,1.217; 107-150,1.215; 257-265,1.202; 488-499,1.188; 9-35,1.178; 363-375,1.157; 269-295,1.153; 308-315,1.147; 474-481,1.128; 344-350,1.111; 297-303,1.101; 455-465,1.099; 421-430,1.091; 192-213,1.086; 97-103,1.074; 178-184,1.033 | Amidation 321-324; Asn_Glycosylation 82-85, 154-157; Camp_Phospho_Site 323-326, 337-340; Ck2_Phospho_Site 184-187, 201-204, 217-220, 340-343, 345-348, 398-401, 446-449; Glycosaminoglycan 328-331; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, 55-60, 67-72, 80-85, 213-218, 331-336, 442-447, 489-494; Pkc_Phospho_Site 84-86, 217-219, 406-408, 446-448, 478-480; Tyr_Phospho_Site 300-306; Pts_Hpr_Ser 474-489; |
| DEX0374_80 .aa.20 | N | 0 -o | 107-148,1.215; 9-35,1.178; 97-103,1.074 | Asn_Glycosylation 82-85; Myristyl 45-50, 48-53, 49-54, 51-56, 52-57, 53-58, 54-59, |

| SequenceID | Signal P | TMHMM | Antigenicity | PTM |
|----------------------|----------|------------------------------|--|--|
| | | | | 55-60, 67-72, 80-85; Pkc_Phospho_Site 84-86; |
| DEX0374_82 .aa.6 | N | 0 -o | 88-110,1.23; 4-77,1.182; 138-159,1.156; 118-136,1.148; 79-86,1.094 | Ck2_Phospho_Site 32-35; Myristyl 13-18, 69-74, 95-100, 136-141; Pkc_Phospho_Site 36-38, 59-61, 82-84; |
| DEX0374_82 .aa.7 | N | 0 -o | 8-56,1.177; 88-100,1.176; 141-149,1.169; 114-122,1.165; 124-133,1.148; 179-186,1.121; 70-82,1.099; 167-174,1.081 | Amidation 170-173; Ck2_Phospho_Site 131-134; Myristyl 19-24; Pkc_Phospho_Site 71-73, 155-157, 158-160, 178-180; |
| DEX0374_82 .aa.9 | N | 1 - i28- 50o | 59-83,1.182; 21-56,1.171 | Asn_Glycosylation 43-46; Ck2_Phospho_Site 12-15, 13-16; |
| DEX0374_85 .aa.5 | N | 2 - o10- 32i64- 86o | 15-50,1.212; 62-91,1.182; 5-11,1.051 | Myristyl 36-41, 47-52, 81-86; Pkc_Phospho_Site 57-59; |
| DEX0374_85 .aa.6 | N | 2 - o10- 32i64- 86o | 15-50,1.212; 62-91,1.182; 5-11,1.051 | Myristyl 36-41, 47-52, 81-86; Pkc_Phospho_Site 57-59; |
| DEX0374_85 .aa.11 | N | 0 -o | 18-30,1.198; 37-49,1.153 | Ck2_Phospho_Site 36-39; Myristyl 56-61, 67-72, 76-81; |
| DEX0374_85 .aa.20 | N | 0 -o | 68-89,1.203; 121-141,1.144; 97-112,1.139; 52-58,1.055; 20-27,1.054; 7-13,1.052 | Ck2_Phospho_Site 97-100, 121-124; Myristyl 58-63, 61-66, 63-68, 64-69; Pkc_Phospho_Site 7-9, 97-99; |
| DEX0374_86 .aa.2 | N | 0 -o | 65-110,1.211; 116-124,1.16; 14-25,1.16; 49-63,1.113 | Ck2_Phospho_Site 15-18, 29-32; Myristyl 105-110; Pkc_Phospho_Site 9-11, 48-50; |
| DEX0374_88 .aa.3 | N | 0 -o | 118-131,1.139; 35-50,1.098; 76-93,1.086; 12-18,1.061 | Asn_Glycosylation 107-110; Camp_Phospho_Site 102-105; Ck2_Phospho_Site 9-12, 24-27; |
| DEX0374_95 .aa.2 | N | 0 -o | 90-119,1.156; 57-67,1.132; 18-29,1.106; 35-51,1.095; 4-10,1.089; 71-77,1.082 | Glycosaminoglycan 19-22, 132-135; Myristyl 58-63, 128-133, 131-136; Pkc_Phospho_Site 19-21, 62-64, 73-75, 132-134; |

Example 2: Relative Quantitation of Gene Expression

Real-Time quantitative PCR with fluorescent Taqman[®] probes is a quantitation detection system utilizing the 5'-3' nuclease activity of Taq DNA polymerase. The method uses an internal fluorescent oligonucleotide probe (Taqman[®]) labeled with a 5' reporter dye and a downstream, 3' quencher dye. During PCR, the 5'-3' nuclease activity of Taq DNA polymerase releases the reporter, whose fluorescence can then be detected by the laser detector of the Model 7700 Sequence Detection System (PE Applied Biosystems, Foster City, CA, USA). Amplification of an endogenous control is used to standardize the amount of sample RNA added to the reaction and normalize for Reverse Transcriptase (RT) efficiency. Either cyclophilin, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), ATPase, or 18S ribosomal RNA (rRNA) is used as this endogenous control. To calculate relative quantitation between all the samples studied, the target RNA levels for one sample were used as the basis for comparative results (calibrator). Quantitation relative to the "calibrator" can be obtained using the comparative method (User Bulletin #2: ABI PRISM 7700 Sequence Detection System).

The tissue distribution and the level of the target gene are evaluated for every sample in normal and cancer tissues. Total RNA is extracted from normal tissues, cancer tissues, and from cancers and the corresponding matched adjacent tissues. Subsequently, first strand cDNA is prepared with reverse transcriptase and the polymerase chain reaction is done using primers and Taqman[®] probes specific to each target gene. The results are analyzed using the ABI PRISM 7700 Sequence Detector. The absolute numbers are relative levels of expression of the target gene in a particular tissue compared to the calibrator tissue.

One of ordinary skill can design appropriate primers. The relative levels of expression of the HSNA versus normal tissues and other cancer tissues can then be determined. All the values are compared to the calibrator. Normal RNA samples are commercially available pools, originated by pooling samples of a particular tissue from different individuals.

The relative levels of expression of the HSNA in pairs of matched samples may also be determined. A matched pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. All the values are compared to the calibrator.

In the analysis of matching samples, the HSNAs that show a high degree of tissue specificity for the tissue of interest. These results confirm the tissue specificity results obtained with normal pooled samples. Further, the level of mRNA expression in cancer samples and the isogenic normal adjacent tissue from the same individual are compared.

- 5 This comparison provides an indication of specificity for the cancer state (e.g. higher levels of mRNA expression in the cancer sample compared to the normal adjacent).

Altogether, the high level of tissue specificity, plus the mRNA overexpression in matched samples tested are indicative of SEQ ID NO: 1-409 being a diagnostic marker for cancer.

10 **Example 3: Protein Expression**

- The HSNA is amplified by polymerase chain reaction (PCR) and the amplified DNA fragment encoding the HSNA is subcloned in pET-21d for expression in *E. coli*. In addition to the HSNA coding sequence, codons for two amino acids, Met-Ala, flanking the NH₂-terminus of the coding sequence of HSNA, and six histidines, flanking the
- 15 COOH-terminus of the coding sequence of HSNA, are incorporated to serve as initiating Met/restriction site and purification tag, respectively.

An over-expressed protein band of the appropriate molecular weight may be observed on a Coomassie blue stained polyacrylamide gel. This protein band is confirmed by Western blot analysis using monoclonal antibody against 6X Histidine tag.

- 20 Large-scale purification of HSP is achieved using cell paste generated from 6-liter bacterial cultures, and purified using immobilized metal affinity chromatography (IMAC). Soluble fractions that are separated from total cell lysate were incubated with a nickel chelating resin. The column is packed and washed with five column volumes of wash buffer. HSP is eluted stepwise with various concentration imidazole buffers.

25 **Example 4: Fusion Proteins**

- The human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector. For example, if pC4 (Accession No.
- 30 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the

present invention, isolated by the PCR protocol described in Example 2, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced. If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if
5 the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. *See, e.g.,* WO 96/34891.

Example 5: Production of an Antibody from a Polypeptide

In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such
10 cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100, µg/ml of streptomycin. The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any
15 suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP20), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands *et al.*, *Gastroenterology* 80: 225-232 (1981).

20 The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide. Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody
25 which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic
30 antibodies to the protein specific antibody and can be used to immunize an animal to induce formation of further protein-specific antibodies.

Example 6: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA is isolated from individual patients or from a family of individuals that have a phenotype of interest. cDNA is then generated from these RNA samples using protocols known in the art. *See*, Sambrook (2001), *supra*. The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO: 1-409. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky *et al.*, *Science* 252(5006): 706-9 (1991). *See also* Sidransky *et al.*, *Science* 278(5340): 1054-9 (1997).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons are also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations are then cloned and sequenced to validate the results of the direct sequencing. PCR products is cloned into T-tailed vectors as described in Holton *et al.*, *Nucleic Acids Res.*, 19: 1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements may also be determined. Genomic clones are nick-translated with digoxigenin deoxyuridine 5' triphosphate (Boehringer Mannheim), and FISH is performed as described in Johnson *et al.*, *Methods Cell Biol.* 35: 73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C-and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. Johnson (1991). Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 7: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

Antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described above. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced. The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbound polypeptide. Next, 50 µl of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbound conjugate. 75 µl of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution are added to each well and incubated 1 hour at room temperature.

The reaction is measured by a microtiter plate reader. A standard curve is prepared, using serial dilutions of a control sample, and polypeptide concentrations are plotted on the X-axis (log scale) and fluorescence or absorbance on the Y-axis (linear scale). The concentration of the polypeptide in the sample is calculated using the standard curve.

Example 8: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1, µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given

continuously, the secreted polypeptide is typically administered at a dose rate of about 1 $\mu\text{g/kg/hour}$ to about 50 mg/kg/hour , either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semipermeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules. Sustained-release matrices include polylactides (U. S. Pat. No. 3,773,919, EP 58,481, the contents of which are hereby incorporated by reference herein in their entirety), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22: 547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15: 167-277 (1981), and R. Langer, Chem. Tech. 12: 98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE Epstein et al., Proc. Natl. Acad. Sci. USA 82: 3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77: 4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324, the contents of which are hereby incorporated by reference herein in their entirety. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation.

For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides. Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably, the carrier is a parenteral carrier, more preferably, a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e. g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container

having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1 % (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container (s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

Example 9: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided above.

Example 10: Method of Treating Increased Levels of the Polypeptide

Antisense or RNAi technology are used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided
5 above.

Example 11: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a
10 subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of
15 the flask and fresh media (e. g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks. pMV-7 (Kirschmeier, P. T. et al.,
20 DNA, 7: 219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using
25 PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 3. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the
30 two fragments. The ligation mixture is then used to transform bacteria HB 101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+aml2 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now
5 produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached
10 producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media.

If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector
15 that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

20 **Example 12: Method of Treatment Using Gene Therapy-In Vivo**

Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide.

25 The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, Tabata H. *et al. Cardiovasc. Res.* 35 (3): 470-479 (1997); Chao J *et al. Pharmacol. Res.* 35 (6): 517-522 (1997); Wolff J. A. *Neuromuscul. Disord.* 7 (5):
30 314-318 (1997), Schwartz B. *et al. Gene Ther.* 3 (5): 405-411 (1996); and Tsurumi Y. *et al. Circulation* 94 (12): 3281-3290 (1996); W0 90/11092, W0 98/11779; U. S. Patent No. 5,693,622; 5,705,151; 5,580,859, the contents of which are hereby incorporated by reference herein in their entirety.

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, hepatic, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

5 The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P. L. *et al. Ann. NY*
10 *Acad. Sci.* 772: 126-139 (1995) and Abdallah B. *et al. Biol. Cell* 85 (1): 1-7 (1995)) which can be prepared by methods well known to those skilled in the art.

 The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art
15 can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

20 The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, hepatic, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide
25 matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They
30 may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin

fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 µg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to hepatics or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle in vivo is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 µm cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection

may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice.

The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

5

Example 13: Transgenic Animals

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e. g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (I. e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., *Appl. Microbiol. Biotechnol.* 40: 691-698 (1994); Carver et al., *Biotechnology* 11: 1263-1270 (1993); Wright et al., *Biotechnology* 9: 830-834 (1991); and U. S. Pat. No. 4,873,191, the contents of which is hereby incorporated by reference herein in its entirety); retrovirus mediated gene transfer into germ lines (Van der Putten et al., *Proc. Natl. Acad. Sci., USA* 82: 6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., *Cell* 56: 313-321 (1989)); electroporation of cells or embryos (Lo, 1983, *Mol Cell. Biol.* 3: 1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e. g., Ulmer et al., *Science* 259: 1745 (1993); introducing nucleic acid constructs into embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm mediated gene transfer (Lavitrano et al., *Cell* 57: 717-723 (1989). For a review of such techniques, see Gordon, "Transgenic Animals," *Intl. Rev. Cytol.* 115: 171-229 (1989).

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., *Nature* 380: 64-66 (1996); Wilmut et al., *Nature* 385: 810813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells,

I. e., mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, e.g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al.,
5 *Proc. Natl. Acad. Sci. USA* 89: 6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some
10 nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et
15 al. (Gu et al., *Science* 265: 103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished
20 by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR (rt-PCR).
25 Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding
30 strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous

transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 14: Knock-Out Animals

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (E. g., see Smithies et al., Nature 317: 230-234 (1985); Thomas & Capecchi, Cell 51: 503-512 (1987); Thompson et al., Cell 5: 313-321 (1989)) Alternatively, RNAi technology may be used. For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (e. g., see Thomas & Capecchi 1987 and Thompson 1989, supra). However, this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e. g., knockouts) are administered to a

patient in vivo. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e. g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc.

The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e. g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, e. g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U. S. Patent No. 5,399,349; and Mulligan & Wilson, U. S. Patent No. 5,460,959, the contents of which are hereby incorporated by reference herein in their entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

While preferred illustrative embodiments of the present invention are described, one skilled in the art will appreciate that the present invention can be practiced by other than the described embodiments, which are presented for purposes of illustration only and not by way of limitation. The present invention is limited only by the claims that follow.

We claim:

1. An isolated nucleic acid molecule comprising:
 - (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 410-611;
 - 5 (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409;
 - (c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b); or
 - (d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b).
- 10 2. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is a cDNA.
- 15 3. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is genomic DNA.
4. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is an RNA.
- 20 5. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is a mammalian nucleic acid molecule.
6. The nucleic acid molecule according to claim 5, wherein the nucleic acid molecule is a human nucleic acid molecule.
- 25 7. A method for determining the presence of a hepatic specific nucleic acid (HSNA) in a sample, comprising the steps of:
 - (a) contacting the sample with the nucleic acid molecule of SEQ ID NO: 1-409 under conditions in which the nucleic acid molecule will selectively hybridize to a hepatic specific nucleic acid; and
 - 30

(b) detecting hybridization of the nucleic acid molecule to a HSNA in the sample, wherein the detection of the hybridization indicates the presence of a HSNA in the sample.

- 5 8. A vector comprising the nucleic acid molecule of claim 1.
9. A host cell comprising the vector according to claim 8.
10. A method for producing a polypeptide encoded by the nucleic acid molecule
10 according to claim 1, comprising the steps of:
- (a) providing a host cell comprising the nucleic acid molecule operably linked
 to one or more expression control sequences, and
- (b) incubating the host cell under conditions in which the polypeptide is
 produced.
- 15
11. A polypeptide encoded by the nucleic acid molecule according to claim 1.
12. An isolated polypeptide selected from the group consisting of:
- (a) a polypeptide comprising an amino acid sequence with at least 95%
20 sequence identity to of SEQ ID NO: 410-611 ; or
- (b) a polypeptide comprising an amino acid sequence encoded by a nucleic
 acid molecule having at least 95% sequence identity to a nucleic acid molecule
 comprising a nucleic acid sequence of SEQ ID NO: 1-409.
- 25 13. An antibody or fragment thereof that specifically binds to:
- (a) a polypeptide comprising an amino acid sequence with at least 95%
 sequence identity to of SEQ ID NO: 410-611 ; or
- (b) a polypeptide comprising an amino acid sequence encoded by a nucleic
 acid molecule having at least 95% sequence identity to a nucleic acid molecule
30 comprising a nucleic acid sequence of SEQ ID NO: 1-409.
14. A method for determining the presence of a hepatic specific protein in a sample,
comprising the steps of:

- (a) contacting the sample with a suitable reagent under conditions in which the reagent will selectively interact with the hepatic specific protein comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 410-611; and
- 5 (b) detecting the interaction of the reagent with a hepatic specific protein in the sample, wherein the detection of binding indicates the presence of a hepatic specific protein in the sample.
15. A method for diagnosing or monitoring the presence and metastases of hepatic cancer in a patient, comprising the steps of:
- 10 (a) determining an amount of:
- (i) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 410-611;
- (ii) a nucleic acid molecule comprising a nucleic acid sequence of SEQ
15 ID NO: 1-409;
- (iii) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (i) or (ii);
- (iv) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (i) or (ii);
- 20 (v) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 410-611 ; or
- (vi) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409
25 and;
- (b) comparing the amount of the determined nucleic acid molecule or the polypeptide in the sample of the patient to the amount of the hepatic specific marker in a normal control; wherein a difference in the amount of the nucleic acid molecule or the polypeptide in the sample compared to the amount of the nucleic
30 acid molecule or the polypeptide in the normal control is associated with the presence of hepatic cancer.

16. A kit for detecting a risk of cancer or presence of cancer in a patient, said kit comprising a means for determining the presence of:

- (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 410-611;
- 5 (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409;
- (c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b); or
- (d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b); or
- 10 (e) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 410-611 ; or
- (f) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409.
- 15

17. A method of treating a patient with hepatic cancer, comprising the step of administering a composition consisting of:

- (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 410-611;
- 20 (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409;
- (c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b);
- 25 (d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b);
- (e) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 410-611 ; or
- (f) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-409;
- 30

to a patient in need thereof, wherein said administration induces an immune response against the hepatic cancer cell expressing the nucleic acid molecule or polypeptide.

18. A vaccine comprising the polypeptide or the nucleic acid encoding the polypeptide of claim 12.

SEQUENCE LISTING

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<120> Compositions and Methods Relating to Hepatic Specific Genes and Proteins

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<213> Homo sapien

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23

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26

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27

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<211> 3003

<212> DNA

<213> Homo sapien

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| atgtccaggg gaacatcact cagaagtttg atgtaagtcc tgtgaagata aatcagatta | 300 |
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31

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32

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<211> 1252

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39

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46

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<213> Homo sapien

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| | |
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| caaggcccaa agaagtaaaa agacttgtct acaggagagt gcctctgagg accaacagga | 180 |
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 <212> DNA
 <213> Homo sapien

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| caaggcccaa agaagtaaaa agacttgtct acaggagagt gcctctgagg accaacagga | 180 |
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51

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 <211> 1817
 <212> DNA
 <213> Homo sapien

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 caaacatatt aatattttat aagcttgcag ttatccaaca cccataaata tattccggga 180
 aattaagcca gtcttttcag ttcacaattg agtgtacctg ggagtctcct tgccctttct 240
 cagaagacat taaaaagaaa agctgtaaat cagtcataag aaaaagaaca tatataatct 300
 ggagtagaat tttgcttcca cttggctaatt tttcatcagt gctatgctcc tgtgggtccc 360
 cggatccaaa tatttcctaa cctttacctt ttcattttgt tgagagtagt agtaatccac 420
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 aacattataa aaggaaaaca ttataaagta attaaatttt aaagccagta tgtgaaagaa 660
 gagatggccc aaagtcttca ttacctctt agagaagaaa ctccattaat gtgtgctcag 720
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 cattttcagt tctgttgtga tcatctttta caacataatt caccctcaac tatttttgga 840
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ccatagtgtg agggcacacg tggcccaaga cggccccag gaaaccgagg ccagacagag 1740
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caggcaacgg tgctaca 1817

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<210> 36
<211> 629
<212> DNA
<213> Homo sapien

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cgccccgcca cccccgcctt gctatttatc ttcttaagtc ttcattgata ttctgtgtga 180
aataagcatg tcttgtactt gctttctgat tcataatttt atgaaagaac ttagtagaaa 240
gaaaagtaag tataaaaata gatattggat tctgtcagaa ggcctagatt tgaaataatg 300
ttttgtactt cggttaagatg gaaaacttag tgattcactg atttcttaga cactctaata 360
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gaataaaata tttacataga tacaaaaaa 629

```

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<210> 37
<211> 405
<212> DNA
<213> Homo sapien

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<400> 37
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gttcagatcc tgattgttcc agttagtaga ctttgggcaa actacataac ccctgaagcg 120

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55

ttacttacct aagacttaga gaggctaagg tcatacacgt tataaagggc agaaccggaa 180
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 actaataaaa cttagcagaa gtggaccact taacagagta tgtagtctc ttcaagctgc 300
 cacctcaaaa caccacaggc tgaggcggga gaattggatg aacctgggag acaaagggtg 360
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<210> 38
 <211> 1823
 <212> DNA
 <213> Homo sapien

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56

| | |
|--|------|
| ttttagaagt acttgctatt tatcttctta agtcttcatt gatattctgt gtgaaataag | 1380 |
| catgtcttgt acttgctttc tgattcataa ttttatgaaa gaacttagta gaaagaaaag | 1440 |
| taagtataaa aatagatatt ggattctgtc agaaggccta gatttgaaat aatgttttgt | 1500 |
| acttcggtaa gatggaaaac ttagtgattc actgatttct tagacactct aatatgat | 1560 |
| gctttctgga aggataaaaac aaatacatat gggaaaaagt acttgagacc aaggccagca | 1620 |
| tcaattccag acatcttcat gttcctaata ggctaaatga agttaaaaac ttatttcaga | 1680 |
| tttttctcat ctgtacctta tatctcataa atttattgca tttttatgt cagtagctta | 1740 |
| gctgtttatt gtctttaaaa taacatgtaa acttcaatgt tctatctgga agcagaataa | 1800 |
| aatatttaca tagatacaaa aaa | 1823 |

<210> 39
 <211> 2038
 <212> DNA
 <213> Homo sapien

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| gtcaaaattg gctgatattt gtacatttta atatatgtat tttttcctga agagctgtaa | 180 |
| ataataattg ggaggggaac agggagcagg tagaggata gaagagccag gaatagcaga | 240 |
| atactggtaa ttattgaaga ttaataatgt ttacatgggtg acttggtcgt agaattctgt | 300 |
| tcattttact taagtttgaa attttctgta ataaaaattt gtaagagggt ccaggggaat | 360 |
| aagcacaggg agaaatgtgt ggatattgaa cttggcatta tatcatttga ttgtcaactt | 420 |
| taaaaataaa aggtaaaata aatataaagc tttttaactt ttttcccaa aataattaag | 480 |
| taggggaaag gggggattg aaaactggct gagagattta gagaactaga aataaaccac | 540 |
| ttgcctaaaa caaacgtaat agaaatagct aaattcaaaa taattaatac ggaattaatt | 600 |
| gcagcagttt tcaaaactgtt aaatagccca gaaaaaatg gatagagggt tgtctcctaa | 660 |
| ttgatttgaa tccatagttt gggattttgt ctacatctga ttctttttaa atgctttctt | 720 |
| ttttaaattt gctttccata tgaggattga tacaattgat tctgaaaggc agctgcagaa | 780 |
| gatcataagt aaacaagatg acttgatgac agtgaaaact aatgaaaactg gatatcagga | 840 |
| agcaatagtg aaagaacctg aaattaacac aactcttcag atgcgtttct ttggaaaaag | 900 |
| aggacaaaga aaacttcatt ataaagaatt tcgaagattt atggaaaatt tacaacaga | 960 |
| gattcaagaa atggaattcc ttcagttttc taaaggtttg agtttcatga gaaaagaaga | 1020 |
| ctttgcagag tggctacttt ttttactaa cactgaaaat aaagatattt attggaaaaa | 1080 |

57

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 cataaatttta ttgcatattt tatgtcagta gcttagctgt ttattgtctt taaaataaca 1980
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<210> 40

<211> 1490

<212> DNA

<213> Homo sapien

<400> 40

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 aaaaactctt actttattag agcatttagt tggatgaatt caagtcattt tgccatttta 600
 caaccactt ggaagacttt gctattgcca tgcagatgtt cagtttagct catcgtcctg 660

58

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| tcagactagc ggagtttaag agagctgtga aagtagcaac aggacaagaa ctctcaaaca | 720 |
| atatttttga cactgtcttt aagatctttg atttggatgg tgatgaatgt cttagtcatg | 780 |
| aagagtttct tggggtgtta aaaaacagaa tgcacgcagg tttatgggta ccacaacatc | 840 |
| agagtataca agaatactgg aagtgtgtga agaaagaaag cattaaagga gtaaaagaag | 900 |
| tctggaaaca agctggaaaa ggtctttttt aataaaagat ataatagtat ggcaattata | 960 |
| ttgttccaaa tgtcaaaatt tgtgattttt tagaagtact tgctatttat cttottaagt | 1020 |
| cttcattgat attctgtgtg aaataagcat gtcttgact tgctttctga ttcataattt | 1080 |
| tatgaaagaa cttagtagaa agaaaagtaa gtataaaaat agatattgga ttctgtcaga | 1140 |
| aggcctagat ttgaaataat gttttgtact tcggtaagat ggaaaactta gtgattcact | 1200 |
| gatttcttag acactctaata atgatatgct ttctggaagg ataaaacaaa tacatatggg | 1260 |
| aaaaagtact tgagaccaag gccagcatca attccagaca tcttcatgtt cctaataggc | 1320 |
| taaatgaagt taaaaactta tttcagattt ttctcatctg taccttatat ctcataaatt | 1380 |
| tattgcataat tttatgtcag tagcttagct gtttattgtc tttaaaataa catgtaaact | 1440 |
| tcaatgttct atctggaagc agaataaaat atttacatag atacaaaaaa | 1490 |

<210> 41
 <211> 1321
 <212> DNA
 <213> Homo sapien

| | |
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| <400> 41 | |
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| ttcaagacca gcctggccaa catggtgaaa ccccatctct actaaaaata caaaaactag | 120 |
| ctgggcgtgg tggcaggcgc ctgtaatccc agctattcag gaggcgcagg caagagaatc | 180 |
| gcttgaaccc gggagacgga ggttgtagt agtcaagatc gtgccattgc actccagcct | 240 |
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| tcatttgtct tgcagtgact ctcatgacat tcgtcggctt atggtttgaa tattttcttc | 360 |
| atgggtattt ttgtttttgt tttacttccc aaataataaa aatttggatt tgcttttact | 420 |
| tctcaaataa tgaaaattta gattaatttc acttagacta tttcacatag ttgataagtt | 480 |
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| actctcaaac aatatttttg acactgtctt taagatcttt gatttggatg gtgatgaatg | 600 |
| tcttagtcat gaagagtttc ttggggtgtt aaaaaacaga atgcatcgag gtttatgggt | 660 |
| accacaacat cagagtatac agaatactg gaagtgtgtg aagaaagaaa gcattaaagg | 720 |
| agtaaaagaa gtctggaaac aagctggaaa aggtcttttt taataaaaga tataatagta | 780 |

59

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 tctcataaat ttattgcata ttttatgtca gtagcttagc tgtttattgt ctttaaaata 1260
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 a 1321

<210> 42
 <211> 1601
 <212> DNA
 <213> Homo sapien

<400> 42
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 caaacatatt aatattttat aagcttgcag ttatccaaca ccataaata tattccggga 180
 aattaagcca gtcttttcag ttcacaattg agtgtaacctg ggagtctoct tgcctttct 240
 cagaagacat taaaaagaaa agctgtaaat cagtcataag aaaaagaaca tatataatct 300
 ggagtagaat tttgcttcca cttggctaatt tttcatcagt gctatgctcc tgtggctccc 360
 cggatccaaa ttttctctaa cctttacott ttcattttgt tgagagtagt agtaatccac 420
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60

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<211> 1344
<212> DNA
<213> Homo sapien

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61

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<210> 44
 <211> 1773
 <212> DNA
 <213> Homo sapien

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 catgaaggag aatattatat gacaccacga gacttcctct tctcagtgat gtttgagcaa 420
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 <211> 756
 <212> DNA
 <213> Homo sapien

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 gggatccaaa cagctggctg tggatcaact tttttcagag accttggcga taaagggcta 540
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 catgttgctt ttaaaatgct ggatacagat ggtaatgaga tgattgaaaa aagggaattt 660
 ttttaaggtaa gtggacgcta attattttag gtttatcata aaatacctgg atgtttgtgt 720
 gataatttta catttccatt aaaatcaaaa ttgtat 756

<210> 46
 <211> 1879
 <212> DNA
 <213> Homo sapien

<400> 46
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 tgtgggaaca agaataaaag agaaaccagg attgactggg aagagacaca aagaaacttt 120

| | |
|--|------|
| gtcaaaattg gctgatattt gtacatttta atatattgtat tttttcctga agagctgtaa | 180 |
| ataataattg ggaggggaac agggagcagg tagaggtata gaagagccag gaatagcaga | 240 |
| atactggtaa ttattgaaga ttaataatgt ttacatggtg acttggtcgt agaattctgt | 300 |
| tcattttact taagtttgaa attttctgta ataaaaattt gtaagaggtt ccaggggaat | 360 |
| aagcacaggg agaaatgtgt ggatattgaa cttggcatta tatcatttga ttgtcaactt | 420 |
| taaaaataaa aggtaaaata aatataaagc tttttaactt ttttcccaa aataattaag | 480 |
| taggggaaag ggggggtattg aaaactggct gagagattta gagaactaga aataaaccac | 540 |
| ttgcctaaaa caaacgtaat agaaatagct aaattcaaaa taattaatac ggaattaatt | 600 |
| gcagcagttt tcaaactggtt aaatagccca gaaaaaatg gatagaggtt tgtctcctaa | 660 |
| ttgatttgaa tccatagttt gggattttgt ctacatctga ttcttttaaa atgctttctt | 720 |
| ttttaaattht gctttccata tgaggattga tacaattgat tctgaaaggc agctgcagaa | 780 |
| gatcataagt aaacaagatg acttgatgac agtgaaaact aatgaaaactg gatatcagga | 840 |
| agcaatagtg aaagaacctg aaattaacac aactcttcag atgcgtttct ttggaaaaag | 900 |
| aggacaaaga aaacttcatt ataaagaatt tcgaagattt atggaaaatt taaaaacaga | 960 |
| gattcaagaa atggaattcc ttcagttttc taaaggtttg agtttcatga gaaaagaaga | 1020 |
| ctttgcagag tggctacttt ttttcactaa cactgaaaat aaagatattt attggaaaaa | 1080 |
| tgtgagagag aagttgtcag caggagaggt tggatataccc ttttattatg catgtgataa | 1140 |
| agatgaaata ataagttaga catgtttaca taaagtaact tctgaattaa ccaagactgt | 1200 |
| gctaccctcg atggtatata aaatcaactt gaggaatgtt ctctacatgc tcttctctg | 1260 |
| taaaggaaaa ctactgccta agacagaatc agtgtagcaa ttacaagttt tccattttcca | 1320 |
| gtaaagtcaa gaataagaca agtatcacta ctgttattta atatcactct gtaaacttta | 1380 |
| accagtccaa attaacaaga ttattttaaaa gagtataaaa atgtgaaagg gggtagtagt | 1440 |
| tgtctttgtt tttatatgat gcaattatat gcctagagaa cccaagagaa tccagtagaa | 1500 |
| aaaccgtaga aacaataaga attcaataaa gtacctgtca caatgctaatt atataagcag | 1560 |
| cagcagctct cctatatata aattacaagt agaaaatgta atgacatgca tatgtgtgtg | 1620 |
| tatatatata cgagatgtat gaaatgatga ttgccaagct attaataatt attcatgtac | 1680 |
| agtgggtgagg tttcaagtga tttttacttt ttttctttat acctttatgt attgttccaa | 1740 |
| aaaaatgttt acaatggaca tgtattttat gtaacttttt aaaaagttac ttctattgta | 1800 |
| agaaaaaaat aaattgcagt agaagaaccc agttataact gcaagataaa tatataacaa | 1860 |
| ttagaaataa atttaacaa | 1879 |

<210> 47
 <211> 570
 <212> DNA
 <213> Homo sapien

<400> 47
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 gtcaaaattg gctgatattt gtacatttta atatatgtat ttttctctga agagctgtaa 180
 ataataattg ggaggggaac agggagcagg tagagggtata gaagagccag gaatagcaga 240
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 tttcagattt ttctcatctg taccttatat ctcataaatt tattgcatat tttatgtcag 480
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 agaataaaat atttacatag atacaaaaaa 570

<210> 48
 <211> 699
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (110)..(110)
 <223> n=a,c,g or t

<220>
 <221> misc_feature
 <222> (159)..(159)
 <223> n=a,c,g or t

<220>
 <221> misc_feature
 <222> (174)..(174)
 <223> n=a,c,g or t

<400> 48
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 aggacagctt ttgatccaca acggacagct tgttgatcna atttcggtag gtancaagcc 180
 tttctatgac aggatgtcca tgtgctggga ctctcctagc tttcaggatc aaataaaaaa 240
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 aaaaacttat ttcagatttt tctcatctgt accttatatc tcataaattt attgcatatt 600
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 tctggaagca gaataaaata tttacataga tacaaaaaa 699

<210> 49
 <211> 1960
 <212> DNA
 <213> Homo sapien

<400> 49
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 <211> 1338
 <212> DNA
 <213> Homo sapien

<400> 50
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tggaagttgg cacctttg 1338

<210> 51
<211> 1220
<212> DNA
<213> Homo sapien

<400> 51
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68

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 acaacaacaa caacgatgac 1220

<210> 52
 <211> 1220
 <212> DNA
 <213> Homo sapien

<400> 52
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<210> 53
 <211> 1067
 <212> DNA
 <213> Homo sapien

<400> 53
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 <212> DNA
 <213> Homo sapien

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70

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| tggaatcggg | aagtgaggaa | tctgacaata | aatggggcag | gaaggagagt | catgaaaatc | 540 |
| tgtgatggca | tttatgattg | ttacaatgac | aaagggcatt | tactgatatt | tagtgggtgc | 600 |
| aaaccagagt | acctatacat | gctacactac | acagtatagt | tttaaacaag | aaagaaatgt | 660 |
| tccatgtcct | acattaattt | gaacatctgg | ctggacatcc | atctgagcct | ggaacccaac | 720 |
| tttgcttaaa | tgaaatgaca | gagtaggttt | tgtaatatat | ggcatttttg | cagagtttta | 780 |
| gtactcacia | aatattaaat | gtagcatcc | accctacct | ctgcttcttg | atcttactat | 840 |
| actgctgtat | aaaagggtga | aagacttctg | atctgatttt | attgctcctg | aattctgact | 900 |
| ttttcatgct | aaataagtgc | aagcatataa | accctttttt | atatccttta | gtatagtcac | 960 |
| agactgaaca | tttacttagt | aaacagatat | tatatattta | ctttcctatt | tccccttttt | 1020 |
| atcctaaata | gaccattttt | taatatatta | tccttgatat | ttttaaaatc | tgtgtaagtt | 1080 |
| atattatcca | gggatttcta | gatttaaaga | gaaaattaca | gaatgcttgt | tatta | 1135 |

<210> 55
 <211> 1134
 <212> DNA
 <213> Homo sapien

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| ctatttcttg | catgtggatt tgtttcataa atgagcatat atatctgcat tagagtgaac 180 |
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| ctttgtttgt | tgatagatgt acataatctc ctcttgctga gtcattctac ttctattcca 300 |
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| aaaagtattg | acttaaaaaa aattaccaa cttagaattt caaacatggt catcaatgtg 420 |
| atgaactccc | cagctttcca agttgtcctg cgtctgctgt tgaccaccta gcatggcttc 480 |
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| aaaccagagt | acctatacat gctacactac acagtatagt tttaaacaag aaagaaatgt 660 |
| tccatgtcct | acattaattt gaacatctgg ctggacatcc atctgagcct ggaacccaac 720 |
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| actgctgtat | aaaagggtga aagacttctg atctgatttt attgctcctg aattctgact 900 |
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71

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 <212> DNA
 <213> Homo sapien

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 gtgc 244

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 <212> DNA
 <213> Homo sapien

<220>
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72

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<210> 60
 <211> 746
 <212> DNA

<213> Homo sapien

<400> 60

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gcgggctctg gaggtgctgg acgggtgcga tccgagagca gaccggggcc ctgcgcgagcc      240
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<210> 61

<211> 949

<212> DNA

<213> Homo sapien

<400> 61

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atccattggt ttttcttgaa ttatatcatc agcttcatag tatgtttcat ttgttgcatt      180
tgatgctgca tttgaattga gggctttggg ttttccattt gacttgcctt cttgagtggg      240
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cccgactcg gctcttccga tctgggctct ggctgcctgg gcgctcagcc ttcgcgcgcc 840
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 <211> 747
 <212> DNA
 <213> Homo sapien

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 agattttctct ccctgccttc acccgccctc agaggctccg cgctccttcg tagggacctc 180
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 <211> 668
 <212> DNA
 <213> Homo sapien

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75

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<210> 64
 <211> 3357
 <212> DNA
 <213> Homo sapien

<400> 64
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| ttctggctcta gaagataacc ttagtacttg gtagaaattt tgacaggcta atgacgaaaa | 1500 |
| gtttgtaacc ctgagctttg catgccaag aaaaaataagg tattcttttt tatatatcag | 1560 |
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 <211> 225
 <212> DNA
 <213> Homo sapien

<400> 66
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<210> 67
 <211> 362
 <212> DNA
 <213> Homo sapien

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<210> 68
 <211> 362

<212> DNA

<213> Homo sapien

<400> 68

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cattaatttt ttattaacat agtgaagtta ttttattttc ttctaacttc cactgctgct      180
gttgaggaat cagttgtcat aattgttggt catttgaaga tgatctgtat ttcttctctg      240
gctggtcata agattttttt atggcatgcc tagatgtgct tttcatttca tttatcttac      300
ttgatatcca ttaccctttc tgtaactatt aaccaatttt tagttttgta attattttcc      360
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<210> 69

<211> 290

<212> DNA

<213> Homo sapien

<400> 69

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gtatttaata gtggctgata ttgtacatgg ccctaatttt tccttgttct gagtcctgat      180
ttttccactc tgataagtat ttgatcccg attagtcatt ggtaaaatag atctattgct      240
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<210> 70

<211> 565

<212> DNA

<213> Homo sapien

<400> 70

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tacattatag aaattctaag gttaattttt taaaaattag gtcttaaaat gcttacattt      180
acaaatctga tcaatagttg caacctcttg ttactgtttg cttttataaa ttgaccatta      240
gatgcttggt ctcatgagtt gacacattga aattatgcaa gggtgaattt tgaaaaatct      300
ctgtcaccat atttaatggt tcaagggaat gaaaggattc tagttacata ggcctaaagg      360
acataatgaa atttaaaatt tgtttccctt agaaaagatt aagatatatt ttcttaaaag      420
atattaagaa aggtattctt ccatatccta agttccctta gtaagtttcc atgattagca      480
tcaattgttg aagtgaagtt aatttatgtg tgtcttaccg aatttactgt ggataaagga      540
tgactcaaat aagtatacac ttggc                                           565

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<210> 71
 <211> 1172
 <212> DNA
 <213> Homo sapien

<400> 71
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 taagtacctt gatgcttcaa cagagctaaa ccaaggctcc acctcttcct aatcatgctc 180
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<210> 72
 <211> 1172
 <212> DNA
 <213> Homo sapien

<400> 72
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80

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gtcatgagct tccatttggt gaactctaca ttgtgactga caaacttggc tgcaccttaa 360
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<210> 73
<211> 381
<212> DNA
<213> Homo sapien

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<400> 73
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ggaagatgag actgcggaag ctcggtgggt ttagtagtgg tagcagcaat agcagcacta 180
gcaacaccca taccagcaca aatagtgtta cagagctagt aaaacctggt gtgtacagac 240
ctctagatac acttggtact gcatcagtaa gcagcaaac agtgaaggaa tccacagaga 300
ttcccaccac catattacaa aaagaaggaa ttgcaagtag tcaattagggt agtcgtagta 360
ctcttaggtc atcaagtcac g 381

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<210> 74
<211> 763
<212> DNA
<213> Homo sapien

<400> 74
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<210> 75
 <211> 2685
 <212> DNA
 <213> Homo sapien

<400> 75
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 aatgaaaaca aaagcattgt ttatgtcttt taaattaaga cattttgggg gagtcagttt 720
 gccttttttt aactgacatt cagaggagaa ttcttgcct cccctcatcc acaaatttat 780
 cttgctcctt cttaaagccg tctttaaata cctagcatgt atatgatctc atagtgtgta 840

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| aaacccgtgg ttccaaaact gtttggaact gtttggtgct gtttttcaag tttgagtagt | 960 |
| gaaggctctt ttcttggttg taccctgaat cctagagata ggaattgggc cttctcacct | 1020 |
| gcttcttgac cccttccctg catgctgatg gtgctttgga tccctgttct ttctggctca | 1080 |
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| tggttaactg tgagccaaaa tacaattgga caattagtct cattatttat tgtgccccat | 1860 |
| tgcaacttta tggttcaata aatatataat tttttacaaa tgtaaaattt tacatttaag | 1920 |
| catttgtaaa gttacagcaa aagatgtacc tgttaataca cagaatgtgt acagattatt | 1980 |
| tgttatgaca ataaaacact caaaataaat ggtcttttagc atctcaaatt ccaactgaaa | 2040 |
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| acaaaaaga agatggggaa gaaaagaagg aaaattttct gatataaata tgttggtcaa | 2340 |
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| tttcttacag tagataagct gctcacattt tgttttgaat gggcatctcc tgaggaaatg | 2520 |
| tagcatgaca ttggtactaa ctgcatgtgt aaatacatca tactggcaaa ccgtaaaata | 2580 |
| taaattatgt atcatcattc atgtagtatc tataatttgt aacagtgggg gggaaagatg | 2640 |

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2685

<210> 76

<211> 4594

<212> DNA

<213> Homo sapien

<400> 76

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| agaacagctc tggatgtttt catgcttaat ccctggattt tcagcaccac agtctgaaca | 120 |
| tggacctcga actttagata atctcattaa tcttccactc aaccttcaag aaactcaagt | 180 |
| cactatagaa gaaatcactc ctcttgtccc cccacaatca ggagataaag ggcaagaaga | 240 |
| tctcacaagc tattttcttg aagcaottct aaaatacata gtcattcagg taaaaagttt | 300 |
| agaatggaag aacaaagaaa accaagaaag gggattttca tttttgtttt cacattttta | 360 |
| gaaatattac ttgccttata tttttccaaa catctgtaag gaaaacagtt tatatcatcc | 420 |
| tatacttgac atcccgaga tgagaccaa gccacattat gtcgtgataa agaaagatgc | 480 |
| tgaaaccaat gaagcaatct attgtacaaa ggagcctttc attaaggctc gtgttattgt | 540 |
| cattcgttgg ctgggttctt tctggctgga gccaaaacca catacaggac ctcatattcc | 600 |
| tgggatggaa ggtgaagtct tgccaaagaa tattcagaga gcagctgcta gtttagtata | 660 |
| cagagaagaa agcaaaaatg ataagtctga taaaacagac agaactacag aacccgaaca | 720 |
| gtctcattcc aatacaagca ctctcacgga gcgagaacct agctcatcta gtctctgtag | 780 |
| tattgatgaa gaacatctca cagacattga aatagttcgc agagtttttt cttctaaaag | 840 |
| gagtaatgta aactttgtga cagagatatt tcgtcaggca tttttattac caatttgtga | 900 |
| agcagcagct atgagaaaag tggtaaaagt atatcaagaa tggatccaac aagaggaaaa | 960 |
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| agttgcctgg atcaaagcaa acctaaatgt gtacatctcc cgagaacttt gggatgactt | 1560 |

| | |
|--|------|
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| accattggat aagctgagtg aacagaaaca aaaaaagcac aaagggaaag gagttggaca | 1740 |
| tgaatttcag aaagtttcag ttgacaagtc attttctaga ggatggagtc gtgatcagcc | 1800 |
| tggccaagcc ccaatgagac agaggagtg c aacaaccact ggttctccag gaaccgaaaa | 1860 |
| ggcgaggagt atagtacggc aaaaaactgt cgccatgaga agccgatcca ttggtgaatg | 1920 |
| tgctctgcca tcggcctata tacgcagtc taaaagtgt cctgttctga tccatacttc | 1980 |
| caaacccttc ttgcctgata ttgttctcac tcccctttct gatgagcttt cagatattga | 2040 |
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| ccaaaaactg cctcctctta atagtatat tggcggcagc agtgctaag ttctgatct | 2280 |
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| tatcacttgt taatcaagct ttcagtgaac cagtttatca aaccattttt tttattttga | 3300 |
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<211> 1155

<212> DNA

<213> Homo sapien

<400> 77

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| | |
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| tgaatgagga gcagccattg cctcgaagta gcagcacttc tgacatcttg gaaccattca | 540 |
| ctgttgaacg agccaaaggt gcagttcctg tcattgacag ttcacccgt catgcaccaa | 600 |
| gcttgacagag ttccacagag gcttcttcaa taactagatc cactgaaagc cacatcactg | 660 |
| atactcatag tagagagtct tctctggaag ttggtgatag catatatgac catctttgtc | 720 |
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99

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102

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105

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112

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115

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125

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| tatacttgac atcccgaga tgagaccaa gccacattat gtcgtgataa agaaagatgc | 480 |
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 <212> DNA
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129

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141

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| cattcgcttg ctggtttctt tctggctgga gccaaaacca catacaggac ctcatattcc | 600 |
| tgggatggaa ggtgaagtct tgccaaagaa tattcagaga gcagctgcta gtttagtacc | 660 |
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143

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154

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156

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| ctcaactaga gtcagacatt tttcaciaag tgaagaaact ggaaatgaag tttttggtgc | 1980 |
| tttgaatgag gagcagccat tgctcgaag tagcagcaat tctgacatct tggaaccatt | 2040 |
| cactgttgaa cgagccaaag gtgcagttcc tgtcattgac agttcatccc gtcatgcacc | 2100 |
| aagcttgcag agttccacag aggcttcttc aataactaga tccactgaaa gccacatcac | 2160 |
| tgatactcat agtagagagt cttctctgga agttggtgat agcatatatg accatctttg | 2220 |
| tcatttaata ggtccagtag aacttgcaga ttcagctttt gaacaaatcc agtacattga | 2280 |
| ccttgaagga gatgatgatc ttctttccac cctgaaagaa tatttttaagg aaaaccagga | 2340 |

159

| | |
|---|------|
| aaatcatagt aaaaatgaga cagggaaaga cccagcttct caggaagtga ctattgcagt | 2400 |
| aaataggggt gaaagattat ccttagataa attagaatgc acagatcagg aaactgaatc | 2460 |
| agaaaatatc acctcttttg ttgggactcc tgaaaacctc cagtttcaga aagaacaaaa | 2520 |
| ctcagctgtc ttcagtagta atatcgcacc taaccagtca gacagttttt ttagaacaca | 2580 |
| aacttctgaa aaatctaagc aactaaacac tgataaacag ccatcagagc ctagttaga | 2640 |
| tagcccttgt gataaag | 2657 |

<210> 102
 <211> 1394
 <212> DNA
 <213> Homo sapien

| | |
|--|------|
| <400> 102 | |
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| agaacagctc tggatgtttt catgcttaat ccctggattt tcagcaccac agtctgaaca | 120 |
| tggacctoga acttttagata atctcattaa tctccactc aaccttcaag aaactcaagt | 180 |
| cactatagaa gaaatcactc ctcttgtccc cccacaatca ggagataaag ggcaagaaga | 240 |
| tctcacaagc tattttcttg aagcacttct aaaatacata gtcattcagg taaaaagttt | 300 |
| agaatggaag aacaaagaaa accaagaaag gggattttca tttttgtttt cacattttaa | 360 |
| gaaatattac ttgccttata tttttccaaa catctgtaag gaaaacagtt tataatcatcc | 420 |
| tatacttgac atcccgcaga tgagaccaa gccacattat gtcgtgataa agaaagatgc | 480 |
| tgaaaccaat gaagcaatct attgtacaaa ggagcctttc attaaggctc gtgttattgt | 540 |
| cattcgttgg ctggtttctt tctggctgga gccaaaacca catacaggac ctcatattcc | 600 |
| tgggatggaa ggtgaagtct tgccaaagaa tattcagaga gcagctgcta gtttagtattc | 660 |
| cagagaagaa agcaaaaatg ataagtctga taaaacagac agaactacag aacccgaaca | 720 |
| gtctcattcc aatacaagca ctctcacgga gcgagaacct agctcatcta gtctctgtag | 780 |
| tattgatgaa gaacatctca cagacattga aatagttcgc agagtttttt cttctaaaag | 840 |
| gagtaatgta aactttgtga cagagatatt tcgtcaggca tttttattac caatttgtga | 900 |
| agcagcagct atgagaaaag tggtaaaagt atatcaagaa tggatccaac aagaggaaaa | 960 |
| acctttgttc atgcaagagc ctgaagaaat tgtgatcact tcttcagacc tcccttgcat | 1020 |
| tgaaaatgtc acagaccatg atatttcaat ggaagaagga gaaaaaagag aagaggaaaa | 1080 |
| tgggaccaat actgctgac atgttcgaaa ttccagttgg gcaaaaaacg gctcctacca | 1140 |
| aggtgctctt cataacgcct ctgaagaagc cacagaacaa aacatacgag ctggtaccca | 1200 |
| ggcagttttg caggtgttta ttataaactc atcaaatata tttcttcttg aacctgcaaa | 1260 |

160

tgaaataaaa aatcttctgg atgaacacac agatatgtgt aaacgcattc ttaacattta 1320
 tcggtacatg gttgtacaag tatcaatgga caaaaagact tggtaaaaaa atttttatcc 1380
 tttatgtcta tgtg 1394

<210> 103
 <211> 1324
 <212> DNA
 <213> Homo sapien

<400> 103
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 tggacctcga acttttagata atctcattaa tcctccactc aaccttcaag aaactcaagt 180
 cactatagaa gaaatcactc ctcttgtccc ccacaaatca ggagataaag ggcaagaaga 240
 tctcacaagc tattttcttg aagcacttct aaaatacata gtcattcagg taaaaagttt 300
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 tatacttgac atcccgaga tgagaccaa gccacattat gtcgtgataa agaaagatgc 480
 tgaaaccaat gaagcaatct attgtacaaa ggagcctttc attaaggctc gtgttattgt 540
 cattcgttgg ctggtttctt tctggctgga gccaaaacca catacaggac ctcatattcc 600
 tgggatggaa ggtgaagtct tgccaaagaa tattcagaga gcagctgcta gtttagtacc 660
 cagagaagaa agcaaaaatg ataatgctga taaaacagac agaactacag aaccgaaca 720
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<210> 104

161

<211> 678

<212> DNA

<213> Homo sapien

<400> 104

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tggcagggat tgggtcccgt ctagccagat attctgtctc tgacaatggg caccatttg      180
tggaagcatt ctcatgctg gcggccctgt gggctttgtg atatgcccc gatctctggc      240
ttcctataat agtccacggg ggatgtgtta tccaggaatt tttaaaacc tccttgaacc      300
tattcatatg tgccagctct tagggtgaca gattccagaa gtcagcaaat atttgaacgc      360
ttagtttatg gctagcactg tgctaagcat tgtcgaagat agaaatgatg cttcataact      420
ggctctggct cttgcttgag cttattcttt tttaggaga caagacttgg ttgcagtgtg      480
ggaaaagggtg ggcagtgaca tcagatgtca cttttagaac accaggcaga ccatgagtgg      540
atcagactca cagtgcaga gctcacagag actaatgtct aaaaacagaa acatattatt      600
aataatttat gttgaaaaat aaaactacca gaccaacac tgatttatcc ccatatgcaa      660
gtctaatagc caaatcgt                                     678

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<210> 105

<211> 675

<212> DNA

<213> Homo sapien

<400> 105

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agggattggg gtcccgctca gccagatatt ctgtctctga caatgggcac ccatttgtgg      180
aagcattctt catgctggcg gccctgtggg ctttgtgata tgcccagat ctctggcttc      240
ctataatagt ccacggggga tgtgttatcc aggaattttt aaaaccctcc ttgaacctat      300
tcatatgtgc cagctcttag ggtgacagat tccagaagtc agcaaattatt tgaacgctta      360
gtttatggct agcactgtgc taagcattgt cgaagataga aatgatgctt cataactggc      420
cttggctctt gcttgagctt attctttttt aaggagacaa gacttgggtg cagttgtgga      480
aaaggtgggc agtgacatca gatgtcacct ttagaacacc aggcagacca tgagtggatc      540
agactcacag tgacagagct cacagagact aatgtctaaa aacagaaaca tattattaat      600
aatttatgtt gaaaaataaa actaccagac ccaacactga tttatcccca tatgcaagtc      660
taatagccaa atcgt                                     675

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162

<210> 106
 <211> 1450
 <212> DNA
 <213> Homo sapien

<400> 106
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 acttagcggt gccgcgtccg agtccggcca tcagtggctg cagatccgga ggccaggagc 180
 tcaaccaccc ttcttcggaa cagggccggc ctgctgctgt gccctcgacg ctcggtgcct 240
 gtatctactc cggggcctag gtcggctccg ggggcggctt aggagaaggc cggcggcgag 300
 atgttcaaaa acacgttcca gagcggttcc ctctccatcc tctacagcat cggcagcaag 360
 cctctgcaaa tctgggacaa aaaggtagcg aatggccaca tcaaaagaat cactgataat 420
 gacatccagt ccctgggtgct agagattgaa gggacaaatg taagcaccac atatatcaca 480
 tgccctgcag accccaagaa gacgctggga attaaacttc ctttcttctg catgattatc 540
 aaaaacctga agaagtattt taccttcgaa gtgcaggtag tagatgacaa gaatgtgcgt 600
 cgtcgctttc gggcaagtaa ctaccagagc accaccggg tcaaaccctt catctgcacc 660
 atgcccagtc ggctggatga cggctggaac cagattcagt tcaacttget agacttcaca 720
 cggcgagcat acggcaccaa ttacatcgag accctcagag tgcagaatcc atccctaaga 780
 caagccaagg agatgccgga gatgacgctg ttccagtcct ggaagagggc ctctagaaga 840
 ttccaggaaaa gggggagaa acgtcacatt cgctctcaa aagaagcatt gccttgacag 900
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 gtggaggacg atgcaaaaac atatttatct tagtttgctc tgctgtagtt ctgttattta 1140
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 aagtgcagtg ggggtaagca gtctgtgag tggcgcatga acgctggagc ttattccgcc 1260
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 ataaggaatt ccagaccaat atttcttctt gcggtttatt ctatgtttta tatattatct 1380
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 tggtttgtaa 1450

<210> 107
 <211> 1301
 <212> DNA
 <213> Homo sapien

163

<220>

<221> misc_feature

<222> (119)..(119)

<223> n=a,c,g or t

<400> 107

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gctcgcttct gtcagtgcac accagcggaa ctgagacata gatgcgctgt gcgcgctcag      180
caggacgtcg gtgctgcgca taggtaatct tcacatcact gggagtcctt aggtcgtcga      240
tccagtgggg gatcgtatct aacgaggaag gccgaccgga gcatcatgta ctaaaattac      300
gctcccaaca cggcttcctc tccatcctct acagcatcgg cagcaagcct ctgcaaattc      360
gggacaaaaa ggtacggaat ggccacatca aaagaatcac tgataatgac atccagtccc      420
tggtgctaga gattgaaggg acaaattgaa gcaccacata tatcacatgc cctgcagacc      480
ccaagaagac gctgggaatt aaacttcctt tccttgtcat gattatcaaa aacctgaaga      540
agtattttac cttcgaagtg caggtagtag atgacaagaa tgtgcgtcgt cgctttcggg      600
caagtaacta ccagagcacc acccgggtca aacccttcac ctgcaccatg cccatgcggc      660
tggatgacgg ctggaaccag attcagttca acttgctaga cttcacacgg cgagcatacg      720
gcaccaatta catcgagacc ctcagagtgc agatccatgc aaattgtcgc atccgacggg      780
tttactttct agacagactc tactcagaag atgagctgcc ggcagagttc aaactgtatc      840
tcccagttca gaacaaggca aagcaataac tggaattgtg actcgagggg tagaccctg      900
gatgtgactc ttctttttta aaggaaacta tgtggaggac gatgcaaaaa catattttatc      960
ttagtttgct ctgctgtagt tctgttattt atacttggtg ttgcttgta tggacaccgg     1020
tgaacatgcc gtaactctgt gactgcattg taagtgcagt gggggtaac agtcctgtga     1080
gtggcgcatg aacgctggag ottattccgc cgctgcccc agtgtggggg gagatacctt     1140
taccatgaac ttacagaatt aaagatggcc cataaggaat tccagaccaa tatttcttcc     1200
tgcggtttat tctatgtttt atatattatc taaatatatg tatatgctgt gtcataactca     1260
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<210> 108

<211> 1146

<212> DNA

<213> Homo sapien

<400> 108

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164

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 acttagcggt gccgcgtccg agtccggcca tcagtggctg cagatccgga ggccaggagc 180
 tcaaccaccc ttcttcggaa cagggccggc ctgctgctgt gccctcgacg ctcggtgcct 240
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<210> 109

<211> 588

<212> DNA

<213> Homo sapien

<400> 109

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 cctgtgagtg gcgcatgaac gctggagctt attccgccgc ctgccccagt gtggggggag 420
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165

ttcttctcctgc ggtttattct atgttttata tattatctaa atatatgtat atgctgtgtc 540
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<210> 110
 <211> 1663
 <212> DNA
 <213> Homo sapien

<400> 110
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 tgccctgcag accccaagaa gacgctggga attaaacttc ctttccttgt catgattatc 540
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166

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<210> 111
 <211> 1566
 <212> DNA
 <213> Homo sapien

<400> 111
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167

ggaattccag accaatatctt cttcctgcgg tttattctat gttttatata ttatctaaat 1500
 atatgtatat gctgtgtcat actcataatc tggaaatgaa taaagtgata tttcctggt 1560
 ttgtaa 1566

<210> 112
 <211> 1156
 <212> DNA
 <213> Homo sapien

<400> 112
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 acttagcggtt gcgcggtccg agtcgggcca tcagtggctg cagatccgga ggccaggagc 180
 tcaaccaccc ttcttcggaa cagggccggc ctgctgctgt gccctcgacg ctcggtgcct 240
 gtatctactc cggggcctag gtcggctccg ggggcggctt aggagaaggc cgccggcgag 300
 atgttcaaaa acacgttcca gagcggttc ctctccatcc tctacagcat cggcagcaag 360
 cctctgcaaa tctgggacaa aaaggtagcg aatggccaca tcaaaagaat cactgatagt 420
 actagatgac aagaatgtgc gtcgtcgctt tcgggcaagt aactaccaga gcaccaccg 480
 ggtcaaacc ttcatctgca ccatgcccac gcggctggat gacggctgga accagattca 540
 gttcaacttg ctagacttca cacggcgagc atacggcacc aattacatcg agaccctcag 600
 agtgagatc catgcaaatt gtcgcatccg acgggtttac ttctcagaca gactctactc 660
 agaagatgag ctgccggcag agttcaaact gtatctccca gttcagaaca aggcaaagca 720
 ataactggaa ttgtgactcg agggatagac ccctggatgt gactcttctt tttaaaagga 780
 aactatgtgg aggacgatgc aaaaacatat ttatcttagt ttgctctgct gtagttctgt 840
 tatttatact tgggtgttgct tgtcatggac accggtgaac atgccgtaac tctgtgactg 900
 cattgtaaat gcagtggggg taagcagtc tgtgagtggc gcatgaacgc tggagcttat 960
 tccgccgcct gcccagtggt ggggggagat acctttacca tgaacttaca gaattaaaga 1020
 tggcccataa ggaattccag accaatatctt cttcctgcgg tttattctat gttttatata 1080
 ttatctaaat atatgtatat gctgtgtcat actcataatc tggaaatgaa taaagtgata 1140
 tttcctggt ttgtaa 1156

<210> 113
 <211> 510
 <212> DNA
 <213> Homo sapien

<400> 113
 ttcgctcata agcccaaagg ctcttaaagg agttttgcaa tgcaatccta atcgtgatga 60

168

| | |
|--|-----|
| tataactcta ttcttaactt atcttagaaa tacattacaa aagaccattc tcaactttct | 120 |
| gaaaacttta atatctttta taaaatctga aagattgaga cgggtgttact aaaagtgtca | 180 |
| cggctcatta aatcttgaat cattaagtca agtaccttgg acaaatcatt ttaaattaaa | 240 |
| agaacaatct ttaatatata ttttcagatg agacttaata cattctacac aacttatcaa | 300 |
| aagccacaga aaagctacgg aaataatgga atgaacacac agtgatattt gcttcaggaa | 360 |
| cagactattt caccctacat ccttttaag tgcttgagat atgcatattt agtaggcata | 420 |
| tttcagaatt agctcttcat tttctaataa aaaaagggca gacttcctg caggcttggc | 480 |
| aatgaaacat tttctaaaat gcaggtacca | 510 |

<210> 114
 <211> 752
 <212> DNA
 <213> Homo sapien

| | |
|--|-----|
| <400> 114 | |
| cggtcgcatg gcgaatccgg ctgatacaca cacgctagga aatcaaacat tcaattccat | 60 |
| aaacataata catctgaagc aaagataatg ccaccaggta ttttttactt tataagttgg | 120 |
| tccccagaaa aggataatta taaaagacac caggaagcct cttttcaacc ttgttaaata | 180 |
| aacgacttgc aaatattaac cacaaaactg tgggtgaagc cactctgtcc tgtcatgatt | 240 |
| actcgctcat aagcccaaag gctcttaaag gagttttgca atgcaatcct aatcgatgat | 300 |
| atataactct attcttaact tatcttagaa atacattaca aaagaccatt ctcaactttc | 360 |
| tgaaaacttt aatatctttt ataaaatctg aaagattgag acggtgttac taaaagtgtc | 420 |
| acggctcatt aaatcttgaa tcattaagtc aagtaccttg gacaaatcat tttaaattaa | 480 |
| aagaacaatc tttaatatac attttcagat gagacttaat acattctaca caacttatca | 540 |
| aaagccacag aaaagctacg gaaataatgg aatgaacaca cagtgatatt tgcttcaggaa | 600 |
| acagactatt tcaccctaca tcctttttaa gtgcttgaga tatgcatatt tagtaggcat | 660 |
| atttcagaat tagctcttca ttttctaata aaaaaagggc agacttcctt gcaggcttgg | 720 |
| caatgaaaca ttttctaaaa tgcaggtacc ag | 752 |

<210> 115
 <211> 751
 <212> DNA
 <213> Homo sapien

| | |
|--|-----|
| <400> 115 | |
| ctacataatc cactgatata cacacactaa gaaatcaaac atttccaatt ccataaacat | 60 |
| aatacatctg aagcaaagat aatgccacca ggtatttttt actttataag ttgggtcccca | 120 |

169

```

gaaaaggata attataaaag acaccaggaa gcctcttttc aaccttgta aataaacgac      180
ttgcaaatat taaccacaaa actgtgggtg aagccactct gtcctgtcat gattactcgc      240
tcataaaggc ccaaaatgcg tcttgaaggg agtttttgca atacaaatcc taatcttaat      300
tatataaact ctattcttaa ctatcttaaa atacattaca aaagaccatt ctcaactttc      360
tgaaaacttt aatatctttt ataaaatctg aaagattgag acggtgttac taaaagtgtc      420
acggctcatt aaatcttgaa tcattaagtc aagtaccttg gacaaatcat tttaaattaa      480
aagaacaatc tttaatatac attttcagat gagacttaat acattctaca caacttatca      540
aaagccacag aaaagctacg gaaataatgg aatgaacaca cagtgatatt tgcttcagga      600
acagactatt tcacctaca tccttttaaa gtgcttgaga tatgcatatt tagtaggcat      660
atttcagaat tagctcttca ttttctaata aaaaaagggc agacttccct gcaggcttgg      720
caatgaaaca ttttcaaat gcaggtagca g                                751

```

```

<210> 116
<211> 428
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (321)..(321)
<223> n=a,c,g or t

```

```

<400> 116
gaaagattga gacggtgtta tcttaaagtg tcacggctgc attaaatcgt tgaatcatta      60
agtcaagtac cttggacaaa tcatttggtta attataaagt acaatcttga atatacattt      120
tcagatgaga ctttaatacat tctacacaac ttatcaaaag cctactagat aaagctacgg      180
aaataatggg aatgatacac acagtgtata tttgcttcag ggacagacta tttcaccctt      240
acatcctttt aaagtgcttg agatatgcat atttagtagg catatttcag tatattagct      300
cttcattttc tatatatata naatataggg ctagacttoc ccgcaggctt ggcgatatgt      360
aaactatttt ctaataatgc aaggtagaca ggtagggtag tgggtggttca tgcactgtaa      420
tctctagc                                428

```

```

<210> 117
<211> 671
<212> DNA
<213> Homo sapien

```

```

<400> 117
ccacagcgcc cggccagcat gtgtttctgt tttccgcagg aagagaatca tgtcgactca      60
caattcacaa tgagtcaacc ggtgtgtaaa atattttaca taatgggaaa atttattgtg      120

```


170

```

acccaaaagt tcagtgtgtt ctcattaagt taccagaaat tacagatgtg aagatactcc 180
tggttaactta accaaaatca agaaaagaaa ctactttaga tacgcacaca ttttcagttt 240
ggtagatctg attcttttta tgatactgca tttcaagtta ctcagattgg taaattcata 300
gcttaaatac taaatagaga aaatctgcat attgacaaca taggtaattt aagactgggt 360
ttggcactgc gtcacttact acctatatag ctaagctctg tcaaacctg acagggacag 420
cttcagtttt tgtaaatact cgcattggtga aatgggtttt ccaaagttat gataccatct 480
aaagtgtctaa tggagccttc ccattgtgct tcacggtgaa taacatattt ctgtggaaaa 540
tcttatagtg ttgcatccat ttaacatttt ccagaatac attcaggttt ttttaatccc 600
gaagaaaaca tttaaacaat taaaacacat aaaatttttc tattatgacc tttaaaaaac 660
ctcagtcctt a 671

```

```

<210> 118
<211> 679
<212> DNA
<213> Homo sapien

```

```

<400> 118
ccacagcgcc cggccagcat gtgtttctgt tttccgcagg aagagaatca tgtcgactca 60
caattcacaa tgagtcaacc ggtgtgtaaa atattttaca taatgggaaa atttattgtg 120
acccaaaagt tcagtgtgtt ctcattaagt taccagaaat tacagatgtg aagatactcc 180
tggttaactta accaaaatca agaaaagaaa ctactttaga tacgcacaca ttttcagttt 240
ggtagatctg attcttttta tgatactgca tttcaagtta ctcagattgg taaattcata 300
gcttaaatac taaatagaga aaatctgcat attgacaaca taggtaattt aagactgggt 360
ttggcactgc gtcacttact acctatatag ctaagctctg tcaaacctg acagggacag 420
cttcagtttt tgtaaatact cgcattggtga aatgggtttt ccaaagttat gataccatct 480
aaagtgtctaa tggagccttc ccattgtgct tcacggtgaa taacatattt ctgtggaaaa 540
tcttatagtg ttgcatccat ttaacatttt ccagaatac attcaggttt ttttaatccc 600
gaagaaaaca tttaaacaat taaaacacat aaaatttttc tattatgacc tttaaaaaaa 660
cctcagtcct ttattttat 679

```

```

<210> 119
<211> 603
<212> DNA
<213> Homo sapien

```

```

<400> 119
ccacaccag ccttattctt tgaaaagtag ctcattgttg catgttggga tttgtgatca 60

```

171

```

catatatatatt tatgatgtaa caaaaggcag ttttgggaaa tattactagt tagctcttca 120
ggtgttttact tgttttaaagc tcttttagttg tttagaagca tctgacttaa cggagtagag 180
ctttgaatgc tgatttaaga ctgacttcag cctgggcgac agagcgaaaa acaaaaaaaaa 240
agctaaagaa aaaagaggtc aaggactccg tccttggaat cctaagaaaa ttttccagcc 300
gtattaccct tctatgaagc ccacctgtca accaacaagc acccactcga tcagagcttc 360
cccaggcttt ttggtgtctc ctcttgcacat gggaattgac ttccaaggac caccagacac 420
tgaggaagta ttttaacata taaagcaaaa gcaacaatag ggcagctgga gaaaggaaat 480
tagaagtaac agagccaatg cagtgattag aaaaacactc aaaaaaatgg taataaatgt 540
gttcaatggg tcaagagaac atatttccat ctatttaaata aaaaacagga atcaataaaa 600
gtg 603

```

```

<210> 120
<211> 616
<212> DNA
<213> Homo sapien

```

```

<400> 120
ccacacccag ccttattctt tgaaaagtag ctcatgtgtg catgttggga tttgtgatca 60
catatatatatt tatgatgtaa caaaaggcag ttttgggaaa tattactagt tagctcttca 120
ggtgttttact tgttttaaagc tcttttagttg tttagaagca tctgacttaa cggagtagag 180
ctttgaatgc tgatttaaga ctgacttcag cctgggcgac agagcgaaaa aaaaaaaaaa 240
agctaaagaa aaggaaaaga ggtcaaggac tccgtccttg gaatcctaag aaaattttcc 300
agccgtatta cccttctatg aagcccacct gtcaaccaac aagcaccacac tcgatcagag 360
cttccccagg ctttttggtg tctctcctt gcattgggaat tgacttccaa ggaccaccag 420
aactgagga agtattttaa catataaagc aaaagcaaca atagggcagc tggagaaagg 480
aaattagaag taacagagcc aatgcagtga ttagaaaaac actcaaaaaa tggtaataaa 540
tgtgttcaat ggtcaagag aacatatttc catctattta aataaaaaa ggaatcaata 600
aaagtgaaaa aaaaaa 616

```

```

<210> 121
<211> 611
<212> DNA
<213> Homo sapien

```

```

<400> 121
atctgcatgt aaaggggtat gatttctgct ctcttttaaa ttaggccaga tgacacgtgt 60
agctttgatt atgtagtgaa acatgtaatc tccttgcttg agtcacacgg gcagagcctg 120
acaccacatc aaaaggccct gagtacagat gaagtagaag gaggaccgaa tggaagaatg 180

```

172

cctcttgtca ttattcgagt gcacgatccc ttgctcgcc ctcaacattc atctctcttt 240
 acgtcttata taaaccagct gtttctcatc tcagtggcct ttctcaagct tctcctctgc 300
 ccagtgtcca tttctgcctt ccttttgccc ttatgatgct ttattttcta ctcatctttg 360
 aatatctgtt ctggtttcac ttcaagtggc ttctctcaga agctgtgctt ggcattcaga 420
 gtgattctat agtgacgcta atgaggctta agtttcaggg ccactccctt gcatgggtcc 480
 tttccaaggc cctgggaggg ccttagcagt gttttcacgt ggctatgttt ttaaaaataa 540
 aatctgtaga ctatatttta aacataattg tctttagact ctccatttca actaccgctc 600
 caagatgggt g 611

<210> 122
 <211> 771
 <212> DNA
 <213> Homo sapien

<400> 122
 atctgcatgt aaaggggtat gatttctgct ctcttttaaa ttaggccaga tgacacgtgt 60
 agctttgatt atgtagtgaa acatgtaate tccttgcttg agtcacacgg gcagagcctg 120
 acaccacatc aaaagggcct gagtacagat gaagtagaag gaggaccgaa tggaagaatg 180
 cctcttgtca ttattcgagt gcacgatccc ttgctcgcc ctcaacattc atctctcttt 240
 acgtcttata taaaccagct gtttctcatc tcagtggcct ttctcaagct tctcctctgc 300
 ccagtgtcca tttctgcctt ccttttgccc ttatgatgct ttattttcta ctcatctttg 360
 aatatctgtt ctggtttcac ttcaagtggc ttctctcaga agctgtgctt ggcattcaga 420
 gtgattctat agtgacgcta atgaggctta agtttcaggg ccactccctt gcatgggtcc 480
 tttccaaggc cctgggaggg ccttagcagt gttttcacgt ggctatgttt ttaaaaataa 540
 aatctgtaga taatatttta accataattg ttttagactc tccatttcaa ctaccgctcc 600
 aagatgggtt ggggggtacc tcctcttctg ataggtggcg ttggaatgac caggacattt 660
 tggggaatca gggtaaagg atgttgagtt tggaatacat tagtttgggt tttagtggaa 720
 taatatattt acgtggttgt taatatagga aatggtgtgg ctgggcacgg t 771

<210> 123
 <211> 1247
 <212> DNA
 <213> Homo sapien

<400> 123
 gagcctacca cgctgctgaa ctgcccaatc tgtgggtcatt ctagtcttca tagacttgaa 60
 agctaagcta tttccagtga taagactacc tgaccacctt atgacaatgg cagggtgaaag 120

173

| | | | | | | |
|------------|-------------|------------|------------|------------|------------|------|
| ttgtagaaaa | tattggaatg | ttcctcttac | gggtgaccag | gagagcagag | tgctgattaa | 180 |
| atgtttcttt | tcctaagtga | cttctattta | ggactgcata | tttttcaggc | ctttctttta | 240 |
| gcagaataaa | aattcaccag | gctctgaatt | gacttatcac | tatggaatac | tgaacttatt | 300 |
| aagattaagt | ctcctaaagt | attgggggaa | ttgaggtatg | ctgggcttac | cttgttctca | 360 |
| ttttgaagga | agctttgggtg | cccctgaaat | gctatgggtg | ttttattacg | atgaaggcta | 420 |
| agttgccctt | gcaacattca | ttgcctacta | atgaggttgt | gtggttaata | gagtttctgc | 480 |
| atctctgtag | tcatacatgt | gccttttgga | catattgaac | tactatacag | ataatttggt | 540 |
| cttttggtcc | ttttattgggt | ttattggctt | aacgatgggt | aaagttgtta | cctgaagttt | 600 |
| ataaatttct | ccttctagga | ttttctgtgg | tttattgtaa | aatgaagaat | cattttttta | 660 |
| gtctttcaat | taaaacctta | tttattgaat | tttcatgtct | taaccatagt | agctaccctg | 720 |
| tattgagaat | agacatatta | atagaatatg | attatgaaaa | tttcagtgtg | ttctgtgggt | 780 |
| agtgtgggtt | gtggatagca | gtcttttgct | attgttacag | gaaacaaatc | tgtacttatt | 840 |
| agaaaaatca | tgtttttact | tttatctgag | ggctaccaa | gatatctggc | tatttaattt | 900 |
| aaaggttttt | ggttgtcttt | ggtaaccatg | atgtcagcat | tatacacaaa | aggtgaaaca | 960 |
| ttgttcacca | aataagtaatc | cattaccaca | gcagagtgat | gggaggtgaa | taagtaatgt | 1020 |
| agttatttct | tatgtttttc | tttgtgaatt | gtagagtatg | ttaataacat | catcattatt | 1080 |
| actggcagaa | atgtaagaag | tagagacaat | tttacatttc | agaaaggact | gattaagtgt | 1140 |
| tatcaggatg | tactgggtgg | atagtgtatt | aaaatggaaa | tgtaacaata | tggaataaat | 1200 |
| aaagctgttt | taccgtgtat | tagaaaatat | ttaaataaaa | ctgatgg | | 1247 |

<210> 124

<211> 1785

<212> DNA

<213> Homo sapien

<400> 124

| | | | | | | |
|------------|------------|------------|-------------|------------|------------|-----|
| atgtcactct | tctgcttaaa | gaccccagtg | actccccatc | tcacttacag | taaaagccat | 60 |
| aggccttatg | gtggcctgca | agacctgcat | aatcattttg | cctgctgcct | ttcttgtaat | 120 |
| tattgtgtca | ttggaacaca | ataatgccca | ttcattttatc | tgttgtctgt | gtttgctttc | 180 |
| tctaaaaatg | caaagttgaa | tagttgtgac | agaaactata | tggcttgcaa | cacctggact | 240 |
| atctcctatt | tgtccctttt | caggaaaagt | ttgtcgaccc | cctgatctag | agcataagat | 300 |
| tcttggtgac | agggactcat | tttaatcgca | gttgatttca | tatcatttca | actgtgattt | 360 |
| ggcatctagt | agatttttta | caattcttga | agggtgga | gatctagata | tatatgacta | 420 |
| gggtgctagt | ttcttttcta | cttctactcc | tttttttcta | ctagtttcta | ctgcaaactt | 480 |

174

```

getcccaagt aaatgcatga tgttacaact tctcagccga tgtcatggag cctaccacgc 540
tgctgaactg cccaatctgt gggtcattcta gtcttcatag acttgaaagc taagctatct 600
ccagtgataa gactacctga ccaccttatg acaatggcag gtgaaagttg tagaaaatat 660
tggaatgttc ctcttacggt gtaccaggag agcagagtgc tgattaaatg tttcttttcc 720
taagtgaactt ctatttagga ctgcatatctt ttcaggcctt tctttaagca gaataaaaat 780
tcaccaggct ctgaattgac ttatcactat ggaatactga acttattaag attaagtctc 840
ctaaagtatt gggggaattg aggtatgctg ggcttacctt gttctcattt tgaaggaagc 900
tttggtgccc ctgaaatgct atgggtggtt tattacgatg aaggctaagt tgccttgca 960
acattcattg cctactaatg aggttgtgtg gtaataagag tttctgcatt tctgtagtca 1020
tacatgtgcc ttttggacat attgaactac tatacagata atttggtctt ttggtccttt 1080
tattggttta ttggcttaac gatgggtaaa gttgttacct gaagtttata aatttctcct 1140
tctaggattt tctgtggttt attgtaaaat gaagaatcat tttttaagtc tttcaattaa 1200
aaccttatct attgaatttt catgtcttaa ccatagtagc taccctgtat tgagaataga 1260
catattaata gaatatgatt atgaaaattt cagtgtattc tgtggttagt gtggttagtg 1320
gatagcagtc ttttgctatt gttacaggaa acaaactctg acttattaga aaaatcatgt 1380
ttttactttt atctgagggc taccaaagat atctggctat ttaatttaaa ggtttttggt 1440
tgtctttggt accatagatg tcagcattat acacaaaagg tgaaacattg ttcaccaaat 1500
agtaatccat taccacagca gagtgatggg aggtgaataa gtaatgtagt tatttcttat 1560
gtttttcttt gtgaattgta gagtatgtta ataacatcat cattattact ggcagaaatg 1620
taagaagtag agacaatttt acatttcaga aaggactgat taagtgttat caggatgtac 1680
tggtggtata gtgtattaaa atggaaatgt aacaatatgg caataataaa gctgttttac 1740
cgtgtattag aaaatattta aataaaaactg atggacaaca aaaaa 1785

```

<210> 125

<211> 2416

<212> DNA

<213> Homo sapien

<400> 125

```

atgaccttca aacctgaag ttaactaaag gttcatatct taaacttctg ttgtttatct 60
acacttatac tttagctgac ctcatcctgt ctcatggttt tatgtacagt actttttaac 120
ttactctcaa atttatatca agtataacct cttccctgaa ctccagagtc atgtctaatt 180
gtctaataatc ttcaacttaa tgaataatgg tcatctcaaa ctactgtat ccaaagctaa 240
aatcctgatt ttctgtccca aaatggctcc ttccatacac ttccatcat atgggggaaga 300

```

175

| | |
|--|------|
| aaaccccatg ctacttggtc aggccacaaa ccttagagtt atccttactc tctcttttca | 360 |
| ccctacatcc aatcccgtag caaatcatga ttataccttc tatatataat cagaatcaaa | 420 |
| ccacgttttg ccactgtcac tgctaccatc cattagtttg caagataaac tcatctctct | 480 |
| cattttgttg caataatttt tgaactgttt tctttgttta tacccttccg attttctggc | 540 |
| atctctaccc ttccattat actctccaca ccgcagctaa ggcatcctt tttgatgatg | 600 |
| atgcttttta agagcaatta tgtcactctt ctgcttaaag accccagtga ctcccatct | 660 |
| cacttacagt aaaagccata ggccattatg tggcctgcaa gaccctgcat aatcattttg | 720 |
| cctgctgcct ttcttgtaat tattgtgtca ttggaacaca ataatgcca ttcatttatc | 780 |
| tgttgtctgt gtttgctttc tctaaaatgt caaagttgaa tagttgtgac agaaactata | 840 |
| tggcttgcaa cacctggact atttcctatt tgtccctttt caggaaaagt ttgctgacct | 900 |
| cctgatctag agcataagat tcttggtgac agggactcat tttaatcgca gttgatttca | 960 |
| tatcatttca actgtgattt ggcatctagt agatttttta aaattcttga aggggtggaca | 1020 |
| gatctagata tatatgaata ggggtgctagt ttcttttcta cttctactcc tttttttcta | 1080 |
| ctagtttcta ctgcaaactt gctcccaagt aaatgcatga tgttacaact tctcagaaga | 1140 |
| tgttcatgga gcctaccacg ctgctgaact gcccaatctg tggtcattct agtcttcata | 1200 |
| gacttgaaag ctaagctatt tccagtgata agactacctg accaccttat gacaatggca | 1260 |
| ggtgaaagtt gtagaaaata ttggaatgtt cctcttacgg tgtaccagga gagcagagtg | 1320 |
| ctgattaaat gtttcttttc ctaagtgact tctatttagg actgcatatt ttccaggcct | 1380 |
| ttctttaagc agaataaaaa ttcaccaggc tctgaattga cttatcacta tggaaactg | 1440 |
| aacttagtta agattaagtc tcctaaagta ttgggggaat tgaggtatgc tgggcttacc | 1500 |
| ttgttctcat tttgaaggaa gctttggtgc ccctgaaatg ctatgggtgg tttattacga | 1560 |
| tgaaggctaa gttgcccttg caacattcat tgcctactaa tgaggttgtg tggtaataag | 1620 |
| agtttctgca tttctgtagt catacatgtg ctttttggac atattgaact actatacaga | 1680 |
| taatttggtc ttttggctct tttattgggt tattggctta acgatgggta aagttgttac | 1740 |
| ctgaagttta taaatttctc cttctaggat tttctgtggt ttattgtaaa atgaagaatc | 1800 |
| attttttaag tctttcaatt aaaaccttat ttattgaatt ttcattgtctt aacctagta | 1860 |
| gctaccctgt attgagaata gacatattaa tagaatatga ttatgaaaat ttcagtgtat | 1920 |
| tctgtggtta gtgtgggttag tggatagcag tcttttgcta ttgttacagg aaacaaatct | 1980 |
| gtacttatta gaaaaatcat gtttttactt ttatctgagg gctaccaaag atatctggct | 2040 |
| atttaattta aaggtttttg gttgtctttg gtaccataga tgtcagcatt atacacaaaa | 2100 |
| ggtgaaacat tgttcaccaa atagtaatcc attaccacag cagagtgatg ggaggtgaat | 2160 |

176

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 <213> Homo sapien

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 gtaagtactt gaaagatgta ttaaaatatg attgggg 217

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177

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<211> 217

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<210> 130

<211> 591

<212> DNA

<213> Homo sapien

<400> 130

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ccaaacatat tttccaaaac tttctaaagt ttctgtctgc ctgggaaaat tttctcatt 240

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<210> 131

<211> 1086

<212> DNA

<213> Homo sapien

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| ccgccccctt cccgaccgc tccaaggcgg ccccgcgct ggggctgcgc ggcaggcgga | 1080 |
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| ttatatgaaa acgcgcatag aaggaggagg gaaaaatata taaacaattt tgtaaaaaga | 2520 |
| gggtgtataa aaatgggtgt tttaaaacaa aatgagggca ggaaaataag agggagtggc | 2580 |

180

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 <212> DNA
 <213> Homo sapien

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181

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<211> 477

<212> DNA

<213> Homo sapien

<400> 134

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<210> 135

<211> 476

<212> DNA

<213> Homo sapien

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182

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<213> Homo sapien

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184

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 <222> (182)..(267)
 <223> n=a,c,g or t

<400> 137
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 tggaaggtta caccatgcaa tgggggtttc gctgcctttg cctgtccacc ccaaagact 120
 cctaacattg gaaagaagtg agttgagtgt acatttaaaa aatactattc taggctgggc 180
 annnnnnnnnn nnnnnnnnnnn nnnnnnnnnnn nnnnnnnnnnn nnnnnnnnnnn nnnnnnnnnnn 240
 nnnnnnnnnnn nnnnnnnnnnn nnnnnnnncta ctcttgtagg cagctgtgaa ctcgatggac 300
 atttattctt accaaatggg gatgttacag cttctctaag acgtggctcc accaccggga 360
 gtccgagtgc tgccaagagg aggtctctac tcggaacgca ggtgccgtct ttacagtgga 420
 gccccaggaa gccgtgcagg tttgaggctc acctgagaag gcggcagtgct tgtgttccta 480
 cctcagggtt cactgcaaac aatgcatacg ctgtagcagt tgccagcttg gtttgtcagt 540
 gctggctctc gtgattgggt ctcagggtgt agttgtagca aagttgcgtg ttaatcagag 600
 agcgtcctgc ccatcccagg gtctcagcag ggctgaggca gcgtttgggg accagatccg 660
 tgctgctcct tggcgatgtg caccacagtc atgggaccag agctaggccc actgtggggc 720
 gagtggacac tcagctgggg gtcccattha tgggacacta aaaaactcag cagtgaacac 780
 gacgttttaa cacggtatgt caagaaatca aaat 814

<210> 138
 <211> 534
 <212> DNA
 <213> Homo sapien

<400> 138
 ctgcattaat tttgatttct tgacataaccg tgttaaaacg tcgtgttcac tgctgagttt 60
 tttagtgtcc cataaatggg acccccagct gagtgtccac tcgcccaca gtgggcctag 120

185

ctctgggtccc atgactgtgg tgcacatcgc caaggagcag cacggatctg gtccccaac 180
gctgcctcag ccctgctgag accctgggat gggcaggacg ctctctgatt aacacgcaac 240
tttgctacaa ctcacacctg agaaccaatc acggagacca gcactgacaa accaagctgg 300
caactgctac agcgtatgca ttgtttgcag tgaaccctga ggtaggaaca cagcactgcc 360
gccttctcag gtgagcctca aacctgcacg gcttcctggg gctccactgt aaagacggca 420
cctgcgttcc gagtagagac ctctcttggg cagcactcgg actcccgggtg gtggagccac 480
gtcttagaga agctgtaaca tcaccatttg gtaagaataa atgtccatcg agtt 534

<210> 139
<211> 410
<212> DNA
<213> Homo sapien

<400> 139
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agacacctga gctatgtcac attcagaaat cttaattagt ttgcagagag caagaaagaa 120
attgcctact ctgcatccca tcttctctgt ttgtgtaaag agcccagtaa aacaagacat 180
agcagctcaa ttcagaaatg tgaagcatgt aaccatgata caagagttac ctatatgatt 240
ttcaacaaaa gaaaacttgg atatatttgg gagctgtgag gccaaagtcac aataatacat 300
tagaaataaa tttaatactg tatagttttt aaagtgttga aatatgagtc ccacaggaaa 360
aggaaaatat aaaagataat aaattagatc aaaaagctgt tacggggaga 410

<210> 140
<211> 419
<212> DNA
<213> Homo sapien

<400> 140
gtaaccctct aggagactag aggagctaca gtgttatgtt ctgggtgggt ggaatgactg 60
agacacctga gctatgtcac attcagaaat cttaattagt ttgcagagag caagaaagaa 120
attgcctact ctgcatccca tcttctctgt ttgtgtaaag agcccagtaa aacaagacat 180
agcagctcaa ttcagaaatg tgaagcatgt aaccatgata caagagttac ctatatgatt 240
ttcaacaaaa gaaaacttgg catatcattt gggcagctgt gaggccaag tcatcaataa 300
tacattagca aataaattta atactgtatc agttttttaa gtgttgaaat atgagtcacca 360
caggataaag gaaatatata aaagataata aattagatca aaaagctgtt acggggaga 419

<210> 141
<211> 411
<212> DNA

186

<213> Homo sapien

<400> 141

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gtaaccctct aggagactag aggagctaca gtgttatgtt ctgggtgggt ggaatgactg      60
agacacctga gctatgtcac attcagaaat cttaattagt ttgcagagag caagaaagaa      120
attgcctact ctgcatccca tcttctctgt ttgtgtaaag agcccagtaa aacaagacat      180
agcagctcaa ttcagaaatg tgaagcatgt aaccatgata caagagttac ctatatgatt      240
ttcaacaaaa gaaaacttgg atatatttgg gagctgtgag gccaaagtcac aataatacat      300
tagaaataaa ttttaactct tatagttttt aaagtgttga aatatgagtc ccacaggaaa      360
aggaaaatat aaaagataat aaattagatc aaaaagctgt tacggggaag a              411

```

<210> 142

<211> 367

<212> DNA

<213> Homo sapien

<400> 142

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cagaaagctt aatgtaaagg tggctgatac tgctgtttcc ttagacactg acaccaaata      60
caataaagaa gtctctcaag aggaaaacat ggtgtgttta caggagcaac taacagttgg      120
tttgtaggca toctaaatgg tggatggcaa gcttgggttt cccaaagggt tctagtcttt      180
atacgtcttc tagtaggtgc ccaggtagt atggcctgtg ttaccagagt aacaatgaaa      240
atggctacgt ctttaaatca ggccacttta cagtgaacta tggtccttaa ttgctatcac      300
atttcaaaca agaactatga ccaattaaac ttactattg ttgaactgcc aaaaaaaaaa      360
aaaaggg                                           367

```

<210> 143

<211> 711

<212> DNA

<213> Homo sapien

<400> 143

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ataaacgagg tagatgttac agttaatgga acatcatgca gottcatatc tcctttttac      60
tcaagctggg gcctatgttt ggtattgaac aaaatggaat gctgcaattt tctctctact      120
gattttgtta ctacagaaag cttaatgtaa aggtggctga tactgctgtt tccttagaca      180
ctgacaccaa atacaataaa gaagtctctc aagaggaaaa catggtgtgt ttacaggagc      240
aactaacagt tggttttag gcatcctaaa tggatggatgg caagcttggg tttcccaaag      300
gtttctagtc tttatacgtc ttctagtagg tgcccagggt agtatggcct gtgttaccag      360
agtaacaatg aaaatggcta cgtctttaaa tcaggccact ttacagtga ctatggctct      420
taattgctat cacatttcaa acaagaacta tgaccaatta aactttacta ttgttgaact      480

```

187

gcctcaagtt ccagaagttt ggtttgtttg atttagattg gtctgtatgg gctcttggtta 540
 aggagtgtac ttggtcttt tgataccatt ctcttggttag tgatcacagt cgtctctctg 600
 ggtgtgttgt accctctcaa gtcttaaata ttgtatgca gccattcatt gagcatcaaa 660
 cggtttcatt ttgactagat tagcaagaat ataaaaaatt atcaactgat g 711

<210> 144
 <211> 483
 <212> DNA
 <213> Homo sapien

<400> 144
 ataaacgagg tagatgttac agttaatgga acatcatgca gcttcatatc tccttttttac 60
 tcaagctggg gcctatgttt ggtattgaac aaaatggaat gctgcaattt tctctctact 120
 gattttgtta ctacagaaag cttaatgtaa aggtggctga tactgctgtt tccttagaca 180
 ctgacaccaa atacaataaa gaagtctctc aagaggaaaa catgggtgtgt ttacaggagc 240
 aactaacagt tggttttag gcatcctaaa tgggtggatgg caagcttggg tttcccaaag 300
 gtttctagtc tttatacgtc ttctagtagg tgcccaggtt agtatggcct gtgttaccag 360
 agtaacaatg aaaatggcta cgtcttttaa tcaggccact ttacagtga ctatggctct 420
 taattgctat cacatttcaa acaagaacta tgaccaatta aactttacta ttgttgaact 480
 gcc 483

<210> 145
 <211> 359
 <212> DNA
 <213> Homo sapien

<400> 145
 cggaaaaaaa agaactagtt taaattctga ctgtatcact gaaaggctgt gtagctgtgt 60
 gaccgtaagc aagtcactta actccagatt ctcatgtctg tcatctataa acagggatga 120
 atgaatatac acctcagagt tgtaagaat ccaatgagaa aatcacgggt aaccttata 180
 taaatgggtg tgaaacattt caaagataca agcatccttg gcctttgcag ccagaatca 240
 tccctccaca ttttctctac aatccaacca catcaagaaa tgataactgc tcagaaagtt 300
 tatcaatatt taccaaaact catggattta aaataaacat taagtttcta ccataaaaa 359

<210> 146
 <211> 1122
 <212> DNA
 <213> Homo sapien

<400> 146
 aaaataaaca ctggccaggc acaggggctc acacctgtaa tcccagcatt ttggggaggcc 60

188

aaggcaggag gatcacttga gcccaggcgt ttaagaccag cctgggcaac atagggagac 120
ccgtttctac aaaaaaagaa aaaattagct gggcttggtg gtacacgcct gtagtcccag 180
ctgcacagga ggctgaggtg ggaggaaggc ttgaggccag gagttcaaga tcagcctggt 240
caacatagca agaccccatc tctacaaaaa agaaaaaaat tagcaaggca tggtaggcatg 300
tgcctgtagt ccctgctact caggaggctg aggcaggagg atcacttgag cccaggagtt 360
caaggctgca gtgagccata atcctgcact gtagcctggg tgacagagtg agtcccccat 420
ctcggaaaaa aaagaactag tttaaattct gactgtatca ctgaaaggct gtgtagctgt 480
gtgaccgtaa gcaagtcact taactccaga ttctcagtgc tgtcatctat aaacagggat 540
gaatgaatat acacctcaga gttgttaaga atccaatgag aaaatcacgg gtaaccctta 600
tataaatggt tgtgaaacat ttcaaagata caagcatcct tggcctttgc agcccagaat 660
catccctcca catttttccct acaatccaac cacatcaaga aatgataact gctcagaaag 720
tttatcaata tttaacaaaa ctcatggatt taaaataaac attaagtttc tacaataagc 780
attcttgtaa ttctatgcca tttgtactcc cttgatcttc accctatttg gcaatatcaa 840
cttttttttt ttgagatgga gtctcacttt gtcaccagg ctggagtgc gtaggtgcaat 900
ctcggctcac tgcaacctcc gcctcccagg ttcaagcaat tctcgtgcct cagcctccca 960
agtagctggg attacaggca cgcaccacca cgtcttgcta atttttgtat ttttagtaga 1020
gatgggtttt taccatgatg gtcaggctgg tcttgaactc ctgacctcag gtgatccacc 1080
cacctcggcc tcccaaagtg ctgggattac aggcgtgagc ca 1122

<210> 147
<211> 283
<212> DNA
<213> Homo sapien

<400> 147
cctagtttct gccactcctg ctgttaaact ttttttttta aaagtttagt agttcacata 60
tgtaaactat taatgcagaa tgaactgctc atttcttccct ccctgagtta cctccatgag 120
acaaatccta gtgtgggatg tcccggaaact accatgcacc tttgccccac cgagtttccc 180
aagaattggt gaaagccttt gctgcagtgg tctgagcagg tgtgctgttg ctgctgcaaa 240
acataccttc atagctgaac tgcttaggaa gccagcagag aag 283

<210> 148
<211> 371
<212> DNA
<213> Homo sapien

<400> 148
cctagtttct gccactcctg ctgttaaact ttttttttta aaagtttagt agttcacata 60

189

tgtaaaactat taatgcagaa tgaactgctc atttcttcct ccctgagtta cctccatgag 120
 acaaatccta gtgtgggatg tcccggaact accatgcacc ttgccccac cgagtttccc 180
 aagaattggt gaaagccttt gctgcagtgg tctgagcagg tgtgctgttg ctgctgcaaa 240
 acataccttc atagctgaac tgcttaggaa gccagcagag aagttttttc ctcccttcct 300
 tccttccttc ctcccttcct tccttcccc ctctccattc cattgtaatt aaagtggcct 360
 agctaagtgc a 371

<210> 149
 <211> 217
 <212> DNA
 <213> Homo sapien

<400> 149
 cctagtttct gccactcctg ctgttaaact ttttttttta aaagtttagt agttcacata 60
 tgtaaaactat taatgcagaa tgaactgctc atttcttcct ccctgagtta cctccatgag 120
 acaaatccta gtgtgggatg tcccggaact accatgcacc ttgccccac cgagtttccc 180
 aagaattggt gaaagccttt gctgcagtgg tctgagc 217

<210> 150
 <211> 879
 <212> DNA
 <213> Homo sapien

<400> 150
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 tggactagac tgtaaaggat taggtaactg aggtgttcaa tatggatact tgttttatgt 120
 ttaatcaaat ttatctgact ctaaataaat ttggctgaaa ctagacagat tccttttcta 180
 ttgagacagt gggctctatt aagcactatg tctgcatagg aaacattaca attaatlttg 240
 cagtgacaat atgcttttta actaacagac taatggaagg aggactgatg taaagcataa 300
 ttctcaaaaa gaggggggta aaaccttggg ttctactaca attattcatt ttatagtatt 360
 gtttgataac acatacttta ttaaattgta gatgcattgt aagtttttat agtatatggg 420
 aatctaaata aaaggagtta ttgggttgtt atgccatatt tagcataaat attaccatcc 480
 atgtatgttg ttgacttaaa acactgttat tttctaaaat gtaagcatag aaaaagaata 540
 aaattcttag ttgatattgc agaaatatat tgtagtgttt gcagcatgaa aaggttttat 600
 atataataat atacacttaa taattaattt ccaaaggctg cctgtgggtca gccttctttg 660
 aaagcatgga ttctggcaaa tgagcaatat aatctcttta agaccattta agctcttaat 720
 ctcttcaaac cagtaccaa gtctgttcat ttgtgtgtaa tagttattgt gtattgtttc 780

190

tttttaattg tgtaagtgag attcaacatc acttgtcaga taagaaaaaa aaccttcaaa 840
 ataaacgtta atttttccca ttattgctag aaggaactt 879

<210> 151
 <211> 879
 <212> DNA
 <213> Homo sapien

<400> 151
 gaaaatgttc cttctgtag aaactttatt aatcccttat gatcttaata ctgttaataa 60
 tggactagac tgtaaaggat taggtaactg aggtgttcaa tatggatact tgttttatgt 120
 ttaatcaaat ttatctgact ctaaataaat ttggctgaaa ctagacagat tccttttcta 180
 ttgagacagt gggctctatt aagcactatg tctgcatagg aacattaca attaattttg 240
 cagtgacaat atgcttttta actaacagac taatggaagg aggactgatg taaagcataa 300
 ttctcaaaaa gaggggggta aaaccttggg ttctactaca attattcatt ttatagtatt 360
 gtttgataac acatacttta ttaaattgta gatgcattgt aagtttttat agtatatggg 420
 aatctaaata aaaggagtta tttggttgtt atgccatatt tagcataaat attaccatcc 480
 atgtatgttg ttgacttaaa aactgttat tttctaaaat gtaagcatag aaaaagaata 540
 aaattcttag ttgatattgc agaaatatat tgtagtgttt gcagcatgaa aaggttttat 600
 atataataat atacacttaa taattaattt ccaaaggctg cctgtggtca gccttctttg 660
 aaagcatgga ttctggcaaa tgagcaatat aatctcttta agaccattta agctcttaat 720
 ctcttcaaac cagtaccaa gtctgttcat tttgttgtaa tagttattgt gtattgtttc 780
 tttttaattg tgtaagtgag attcaacatc acttgtcaga taagaaaaaa aaccttcaaa 840
 ataaacgtta atttttccca ttattgctag aaggaactt 879

<210> 152
 <211> 360
 <212> DNA
 <213> Homo sapien

<400> 152
 ggtattgatt tgagtattat tagtaattaa tctccttgtc taggtttctt cacatacaaa 60
 tttccaagta ttgttcaaag gaagtctgta agatttaggc cattgtttta caaaatacaa 120
 atatttggct tggtgagaat gtcttcctat agataactaa gaaactttta gacttgtgga 180
 tgttctttta attactgtct aatgaatgca cagtaaaatc aaagatcaac caagtatagc 240
 aaattgcagc agcatatttt agaaaggatg ttatataaga agcaaggata cctgaatcct 300
 agtcttggct tcaatagtta ctagctccag acacaggata cagtgttaact ttgggtgatt 360

191

<210> 153
 <211> 360
 <212> DNA
 <213> Homo sapien

<400> 153
 ggtattgatt tgagtattat tagtaattaa tctccttgct taggtttctt cacatacaaa 60
 tttccaagta ttgttcaaag gaagtctgta agatttaggc cattgtttta caaaatataca 120
 atatttggtc ttgttgagaat gtcttcctat agataactaa gaaactttta gacttggtga 180
 tgttctttta attactgtct aatgaatgca cagtaaaatc aaagatcaac caagtatagc 240
 aaattgcagc agcatatttt agaaaggatg ttatataaga agcaaggata cctgaatcct 300
 agtcttggtc tcaatagtta ctatctccag acacaggata cagtgttaact ttgggtgatt 360

<210> 154
 <211> 150
 <212> DNA
 <213> Homo sapien

<400> 154
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 gtacttgagt aagctgtcat ctctagtcaa aaaagggccca cttggatcta ttttaaattt 120
 agggccagtg gccgggcacg gtggctcact 150

<210> 155
 <211> 150
 <212> DNA
 <213> Homo sapien

<400> 155
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 gtacttgagt aagctgtcat ctctaggcaa aaaagggccca cttggatcta ttttaaattt 120
 agggccagtg gccgggcacg gtggctcact 150

<210> 156
 <211> 129
 <212> DNA
 <213> Homo sapien

<400> 156
 gattgggttg ttcgggtgag ctctgaaagc cctaaaaaga aaaagggtgct gggttttcagg 60
 gtacttgagt aagctgtcat ctctagtcaa aaaagggccca cttggatcta ttttaaattt 120
 agggccagt 129

<210> 157
 <211> 612
 <212> DNA

192

<213> Homo sapien

<400> 157

| | |
|---|-----|
| tgccccagcc tgctgtgtga ccttagtcat gtagcttacc ctctctgggc aacttttctt | 60 |
| tctccatcta taaaatgaag gggtagact gggcaacac tgagcctccc cctgagtctg | 120 |
| agtctttgtt gtctgtagat ctgcctgatt tgggggtggct ctgctgggtac tcccacttcc | 180 |
| tgctccatat ctacctcccc ttggatatccc acattgtctc ctgcatgtct tgttgcccca | 240 |
| gggccctgac tggtagtacct ataattaact cctgcccattg ctgaggacat ggagggcctg | 300 |
| cttggtcttg ccagaccag tggcctgttg gggcccgagg cccaccctca cggactggcc | 360 |
| agcgttccca accccagggc cagggcaagg cgtctgtctc cacagtggct acctccagcc | 420 |
| ggcccagcac attcctcagg cttatctgga ggcccgcccc actggactct gccctccac | 480 |
| ccaggaagca gcaccagag ctgcgtgcgg aagagttgca gggcctggga acaggccctg | 540 |
| cgtgagctcg aggtagtgt tcttagcctg gggctggaga gaaacaggta gaggaccggg | 600 |
| tggggcagga gg | 612 |

<210> 158

<211> 614

<212> DNA

<213> Homo sapien

<400> 158

| | |
|--|-----|
| tgccccaggc ctgctgtgtg accttagtca ttagcttac cctctctggg caacttttct | 60 |
| ttctccatct ataaaatgaa ggggttagac tgggtcaaca ctgagcctcc ccctgagtct | 120 |
| gagtctttgt tgtctgtaga tctgcctgat ttgggggtggc tctgctggta ctcccacttc | 180 |
| ctgctccata tctacctccc cttggatatcc cacattgtct cctgcatgtc ttgttgcccc | 240 |
| agggccctga ctggtactcc tataattaac tctgcccatt gctcaggaca tggagggcct | 300 |
| gcttggtctg gccagaccca gtggcctgtt. gggggccggg cccaccctc acggactggc | 360 |
| cagcgttccc aaccaccagg ccagggcaag gcgtctgtc ccacagtggc tacctccagc | 420 |
| cggcccagca cattcctcag gcttatctgg agggccgccc cactggactc tgccctccca | 480 |
| cccaggaagc agcaccaga gctgcgtgcg gaagagttgc agggcctggg aacaggccct | 540 |
| gcgtgagctc gaggtagtga ttcttagcct ggggctggag agaaacagg agaggaccgg | 600 |
| gtggggcagg aggg | 614 |

<210> 159

<211> 258

<212> DNA

<213> Homo sapien

<400> 159

193

| | |
|--|-----|
| gtgagattga aagtcagcaa atgcaaactc attttattgg aagcgggtga gaggccgtga | 60 |
| gcggtggttag taacaggatg aataaactca gcctctgcct tcttcctgta gctgggacag | 120 |
| ccatgaaagc ctccagtcca aatgcaaagg caagtgggta ggacaggcct tctgtggtcc | 180 |
| tcagtcagcc tccttccttg gccactcctg ccattgtgca gtggactcct gggcagaggc | 240 |
| cttctcagta aggcagga | 258 |

<210> 160
 <211> 259
 <212> DNA
 <213> Homo sapien

| | |
|--|-----|
| <400> 160 | |
| gtgagattga aagtcagcaa atgcaaactc attttattgg aagcgggtga gatgccgtga | 60 |
| gcggtggttag taacaggatg aataaactca gcctctgcct tcttcctgta gctgggacag | 120 |
| ccatgaaagc ctccagtcca aatgcaaagg caagtgggta ggacaggcct tctgtggtcc | 180 |
| tcagtcagcc tccttccttg gccactcctg ccattgtgca gtggactcct gggcagaggc | 240 |
| cttctcagta aggcaggag | 259 |

<210> 161
 <211> 148
 <212> DNA
 <213> Homo sapien

| | |
|---|-----|
| <400> 161 | |
| ggttgagatg ccgtgagcgg tggtagtaac aggatagaat caacattcag acctctgact | 60 |
| tcttcctgta gctgggacag accatgacag cctccagtcc aaatgcaaag tggcaagtgg | 120 |
| gataggacag agccgttctg tggtcctc | 148 |

<210> 162
 <211> 337
 <212> DNA
 <213> Homo sapien

| | |
|---|-----|
| <400> 162 | |
| catacagtag cagtaattga aaggatattt catttatata gcatctgtca gcctgaagta | 60 |
| ctttcagagt cttcacaaac aggaactgct ttccttctca gaaaaaatg ctgctaagtt | 120 |
| gaagatggaa ctgaggcagg ctccaggaa cctaactaaa taaaaaactg aatgaactat | 180 |
| tgtggtaaat gggagcaggc gctcttcatt ttatgagata gatgaattac tgaaaaaat | 240 |
| acacagacat ggagtttctt ggggaagtca attaaaaaca aaatcccagt actgtagtag | 300 |
| ttggtcattt aaaagaaaat tgttggccgg gcgcgggt | 337 |

<210> 163

194

<211> 337
 <212> DNA
 <213> Homo sapien

<400> 163
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 ctttcagagt cttcacaaac aggaactgct ttcttctca gaaaaaatg ctgctaagtt 120
 gaagatggaa ctgaggcagg ctccaggaac cctaactaaa tacaaaactg aatgaactat 180
 tgtggtaaata gggagcaggc gctcttcatt ttatgagata gatgaattac tgaaaaaat 240
 acacagacat ggagtttctt ggggaagtca attaaaaaca aaatcccagt actgtagtag 300
 ttggtcattt aaaagaaaat tgttgccgg ggcgggt 337

<210> 164
 <211> 720
 <212> DNA
 <213> Homo sapien

<400> 164
 cactataaat tcagcaatca aaagctgaac aggcagggca aggtcaggtg ctgttaggca 60
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 cctgtctctc tgtggtagac ccacagcact cttcagatgc ccaactgggcc cctggccttt 180
 actttctagt ctaggagact gaggtctaaa ggaaagaaat ggctgcctg cagccatcca 240
 cggaagatgc aaaagagacc acaaatagag tccagggtgcc tgggccctct tttgccccaa 300
 ggctcctcc ccacagaagg tcccatggat cacttcccct tgaacgccag cactaggact 360
 gcctgggtag ctgatataga tggagacgca caatcctctt ggcccagatg gggaactgag 420
 ccgcaagcag tggctcggca gccactaagg ccgaggttta gaaaagtacc actcttgcca 480
 agaaggaatg tgagggaaaag gccaggaggc tgggcgatgc tgggtggtgtg actttgagct 540
 ggcgtcgtgg tttgtggcgt cctcagacca agcagcggca gcacggcaca aaggttgggg 600
 catggcttct tcacaccag ctctccact cacatgtgct gcaaccccg gcaagccgct 660
 tgctcctg aacctcagtt ttctcatcca taaaatgagg tttaggatca taagactgcc 720

<210> 165
 <211> 800
 <212> DNA
 <213> Homo sapien

<400> 165
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 cctgtctctc tgtggtagac ccacagcact cttcagatgc ccaactgggcc cctggccttt 180

195

actttctagt ctaggagact gaggtctaaa ggaaagaaat ggcttgctg cagccatcca 240
 cggaagatgc aaaagagacc acaaataagag tccaggtgcc tgggcectct tttgccccaa 300
 ggctcctcc ccacagaagg tcccatggat cacttcccct tgaacgccag cactaggact 360
 gcctgggtag ctgatataga tggagacgca caatcctctt ggcccagatg gggaactgag 420
 ccgcaagcag tggctcggca gccactaagg ccgaggttta gaaaagtacc actcttgcca 480
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 ggcgctcgtgg tttgtggcgt cctcagacca agcagcggca gcacggcaca aaggttgggg 600
 catggcttct tcacaccag ctctccact cacatgtgct gcaaccccg gcaagccgct 660
 tgctccctg aacctcagtt ttctcatcca taaaatgagg tttaggatca taagactgcc 720
 ttggctgggc gtagtggctc acgcctgtaa tcccagccat tcgggagttt gaggcaggag 780
 aatggcgtga acccgggagg 800

<210> 166
 <211> 781
 <212> DNA
 <213> Homo sapien

<400> 166
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 cccacagcac tcttcagatg ccactggtc ccctggcctt tactttctag tctaggagac 180
 tgaggctcaa aggaaagaaa tggcctgcct gcagccatcc acggaagatg caaaagagac 240
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 g 781

<210> 167
 <211> 1095
 <212> DNA

196

<213> Homo sapien

<400> 167

| | | | | | | |
|-------------|-------------|------------|------------|------------|------------|------|
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| gtctttggat | agtcagccac | atctatggtc | tccaagggcc | ctttctcctc | gccgctgcta | 120 |
| tgggagcctc | aatgagagaa | ccagggattc | tgtacatcat | gtagccctgg | atctggcgct | 180 |
| ggtgctcogt | ctctaaggcc | cttgctcgtg | ctcaggcagg | ggctcacttc | gacatcgctc | 240 |
| cctccctcat | ttcttgccctg | ctacagccaa | gggagccaat | gatctcccg | agcaaaaact | 300 |
| cagcctcccg | ctgcttttcc | ctcattgaag | caggtgtaaa | ttaggaggaa | atggatctgt | 360 |
| ctaagttttt | ggtccaaccc | caataaaaag | ctcatccaac | tggtgtttat | gagccccaag | 420 |
| cctggagggga | gaggccgtga | tttctaatta | ctgaacaatg | agcctttgat | cagactaata | 480 |
| aagagtcatt | tccaagttat | gtagttgggc | tcacagggac | tgggagtcag | aagactcggt | 540 |
| tgataatttt | ttttattgtg | ttaatgagca | gatggatgga | gcttcaggct | agcagataat | 600 |
| tcacagggaa | taatcccat | taccctgtgt | gtgacagaga | tgtgttcaa | gatgggacga | 660 |
| tgtgttgtcg | cccagctggt | ggcagggtaa | gctgtggctt | caagccctct | ctcctctcca | 720 |
| tttttgttca | tttgtttgcc | accatccatc | cctatgaccg | actggcaaag | gacacaggct | 780 |
| tcattccagta | ctagccatgt | ggccttgggg | aggtcacttt | ccccctgggg | tctcatcta | 840 |
| tgaaatgatg | atgatgatta | tagtagtcaa | ttcctgggac | tgctataatg | actgcattgg | 900 |
| gtaatctatg | tggaaggatt | tatttagcca | aatggggatt | ccatatttat | tggctgggtg | 960 |
| tgcttactaa | gcacctccta | tttgccaggc | tttgggggtc | tcatggggag | aaatacatgg | 1020 |
| agcatgggct | ccattcctga | tctgctttt | aagagtgata | cttcctctcc | ctctccctct | 1080 |
| ccctctccct | ctccc | | | | | 1095 |

<210> 168

<211> 1423

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (246)..(328)

<223> n=a,c,g or t

<400> 168

| | | | | | | |
|------------|------------|------------|------------|------------|-------------|-----|
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| tgaagaatga | agacatttct | gctctcagct | ccgggggtga | ggtgtgcctg | gcctctgcct | 120 |
| ccacctcct | cctcttcacc | aggtgcatgc | atgccctctc | tgagtctgga | ctttgcttcc | 180 |
| cctccaggag | ggaccaccct | ccctgactgg | cctgggatat | ctttacaagc | aggcaactgta | 240 |

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tttttnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn    300
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cactgcctgc cctcttctga cctcaggggt ctttggatag tcagccacat ctatggtctc    420
caaggcccct ttctcatcgc cgctgctatg ggagcctcaa tgagagaacc agggattctg    480
tacatcatgt agccctggat ctggcgctgg tgctccgtct ctaaggccct tgtcctgtct    540
caggcagggg ctacttcga catcgctccc tccctcattt cttgctgct acagccaagg    600
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catccaactg ttgtttatga gcccgaagcc tggagggaga ggccgtgatt tctaattact    780
gaacaatgag cctttgatca gactaataaa gagtcatttc caagttatgt agttgggctc    840
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tggatggagc ttcaggctag cagataattc acaggggaata atcccattta ccctgtgtgt    960
gacagagatg tgttccaaga tgggacgatg tgttgctgcc cagctgggtg cagggtgaagc   1020
tgtggcttca agccctctct cctctccatt tttgttcatt tgtttgccac catccatccc   1080
tatgaccgac tggcaaagga cacaggcttc atccagtact agccatgtgg ccttgggaag   1140
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cctgggactg ctataatgac tgcattgggt aatctatgtg gaaggattta tttagccaaa   1260
tggggattcc atatttattg gctgggtgtg cttactaagc acctcctatt tgccaggctt   1320
tggggtcctc atggggagaa atacatggag catgggctcc attcctgac cgtcttttaa   1380
gagtgatact tcctctccct ctccctctcc ctctccctct ccc                      1423

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<210> 169
 <211> 1033
 <212> DNA
 <213> Homo sapien

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<400> 169
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tgctccgtct ctaaggccct tgtcctgtct caggcagggg ctacttcga catcgctccc    180
tccctcattt cttgctgct acagccaagg gagccaatga tctcccgag caaaaactca    240
gcctccgct gcttttccct cattgaagca ggtgtaaatt aggaggaaat ggatctgtct    300
aagtttttgg tccaacccca ataaaaagct catccaactg ttgtttatga gcccgaagcc    360
tggagggaga ggccgtgatt tctaattact gaacaatgag cctttgatca gactaataaa    420

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198

gagtcatttc caagttatgt agttgggctc ccagggactg ggagtcagaa gactcgtttg 480
 ataatttttt ttattgtgtt aatgagcaga tggatggagc ttcaggctag cagataattc 540
 acaggggaata atcccattta ccctgtgtgt gacagagatg tgttccaaga tgggacgatg 600
 tgttgtcgcc cagctgggtg cagggtaagc tgtggcttca agccctctct cctctccatt. 660
 tttgttcatt tgtttgccac catccatccc tatgaccgac tggcaaagga cacaggcttc 720
 atccagtact agccatgtgg ccttgggaag gtcactttcc ccctggggtc ctcatctatg 780
 aaatgatgat gatgattata gtagtcaatt cctgggactg ctataatgac tgcattgggt 840
 aatctatgtg gaaggattta tttagccaaa tggggattcc atatttattg gctgggtgtg 900
 cttactaagc acctcctatt tgccaggctt tggggctctc atggggagaa atacatggag 960
 catgggctcc attcctgac ctagcttttaa gagtgatact tcctctccct ctccctctcc 1020
 ctctccctct ccc 1033

<210> 170
 <211> 524
 <212> DNA
 <213> Homo sapien

<400> 170
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 ggcatggaga aactcaaaact tcccatgttt ttccagtcaa ataataatcc atcccttgcc 180
 atctcctgga ctctaaatgt ttcaaagtac aatatgaaaa agaaaaatct gagccaccac 240
 gccagccaa ccccttggtg tattgacttg ctgagtgcac caggcaatgg ttgtggacac 300
 aatgtggtct catgggagag ctctgtata caaggatatag taatgaggga gcgtctggtt 360
 aacaggattg gcgttcacct tccttggcat tcctaattct tgtagtgaga catgtttttt 420
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 ccgaaatacc cattgaggta gagtcctag tccttttgag aagc 524

<210> 171
 <211> 524
 <212> DNA
 <213> Homo sapien

<400> 171
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 ctacaaagat taggaatgcc aaggaagggtg aacgccaatc ctgttaacca gacgtccct 180

199

cattactata ccttgatatac aggagctctc ccatgagacc acattgtgtc cacaaccatt 240
gcctgatgca ctcagcaagt caatacacca aggggttggc tgggcgtggt ggctcagatt 300
tttctttttc atattgtact ttgaaacatt tagagtccag ggagatggca agggatggat 360
tattatttga ctggaaaaac atgggaagtt tgagtttctc catgcctact ccctgttggt 420
aattgtgttc catatcccaa ggatgaaatt tcaaacaaga aatagaatgc cttttgtttt 480
ccttggagct tagcaagttg aagtcttcta agtcctgtga ggtc 524

<210> 172

<211> 934

<212> DNA

<213> Homo sapien

<400> 172

tgtttgcttt tatgaattgg aggactgcct gggcccaggg aagccgctat tcatctgcct 60
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ctttcttggg cccctctgca cgtgggcagt ccttccatga tgacagctgc cctgttatgg 180
tgggattact ttggaggggtg gatgtggccc aggggaagtgt gtactctcag tgggcaggcc 240
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ctgaaccgat tccttcctat atgtcctcag cttgagtcac tttctgtagc tccctcttat 420
ttccatcaga tacttggata cattttaaat tgtatcccc aaatatcagt gagagaaatc 480
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tttcttgggg gtcttctggg tgtgagcgta gtgagtgtga atgcatcaag gtgcctaaaa 840
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cgcaggaaaa gtgtattaaa ataattctta aaaa 934

<210> 173

<211> 1129

<212> DNA

<213> Homo sapien

<400> 173

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200

actcactacg ctcacaccca gaagaccccc aagaaatccg cttctttgtg cagataaagg 180
 aaatgcaaac tggtcattct ggaaaccagg gtcaattcta gatttctaga agcctggctg 240
 tgggcctcaa ggcctttcat gaaagcaagg gcctcagatt gaccctttcc aagcatcccc 300
 taccaggagg ggaagggcac agattctcaa gggaccgtgg tgcattgcagg taaaccgaaa 360
 cctctaggct ggcacgtggc accactgccc tgggagacaa gccatccccg ctctctgtct 420
 ggatggcctg gtcaatgcag tgtagatcat ggatgtgatt tctctcactg atatttgggg 480
 gatacaattt aaaatgtatc caagtatctg atggaaataa gagggagcta cagaaaatga 540
 ctcaagctga ggacatatag gaaggaatcg gttcagggtg aaggaaggat ttctggggaa 600
 ctttcttctc tgtgttcac cctccctctt tacataaggt cttgagtcac gagcaccttg 660
 tgttagatgc tgggctacaa aatgatcaaa acagaaggcc tgccactga gactacacac 720
 ttccctgggc cacatccacc ctccaaagta atcccaccat aacagggcag ctgtcatcat 780
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 tggtagcatg cgctgtaat ccagctact caggaggttg aggcaggag 1129

<210> 174
 <211> 96
 <212> DNA
 <213> Homo sapien

<400> 174
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 acaataaaag taataaaaaa taccatatta caacta 96

<210> 175
 <211> 96
 <212> DNA
 <213> Homo sapien

<400> 175
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 acaataaaag taataaaaaa taccatatta caacta 96

<210> 176
 <211> 780
 <212> DNA

201

<213> Homo sapien

<400> 176

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agccaagtga gacagggacc catccacatc ccccttagag atcaaacaat tgtgtctcga      60
agcagcaaac ctcccttctca gccatcacct gctgggcatg ttctgggtga gcctggggaa    120
gatgatatgt gcccacatcgt taaaagtgaag agaacgtgca tctcaggggc tccacagagc    180
accagagatc cagtgtctgca gaggcaggat gggcccaggc ccctcaagcc cattcttctc    240
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ggaatgacag gggtttggcaa tcccatagct tctgaattcc agggagggga ggagaaagat     360
gcgggtgaaa acctgctttc agagggtttt cccttggtg cctcctcaac caaactcacc     420
cacaaattgc atgtcaagtt tcccaacctc cacctaaggg agcaggctct ttcacttcag     480
agaattcaga ggcattctga gggcatatgc cagggcaggc acagagttag gaggtggggt      540
tgggggtttt tggacagctc tgggtccctc cagccccaca gagcatgcaa tgtggctgat     600
gctgtctggag agctggtctc tgaaaggaga atgcatgaat ctgaactaga aacagaaggg     660
cagaaggacc aggaaaagaa atgagagcca aacagagtct gagcaatgaa aggatgtttc     720
agagagctga aaacacaagc taagctaagc atcagtggac tgggagagct ctgcaaaata     780

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<210> 177

<211> 839

<212> DNA

<213> Homo sapien

<400> 177

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gccaagttag acagggaccc atccacatcc cccttagaga tcaaacaatt gtgtctcgaa     120
gcagcaaaacc tccttctcag ccatcacctg ctgggcatgt tctgggtgag cctggggaag     180
atgatatgtg ccccatcgtt aaaagtgaag gaacgtgcat ctcaggggct ccacagagca     240
cccagagtcc agtgctgcag aggcaggatg ggcccaggcc cctcaagccc attcttctct     300
tggctcctgt tccatctcgg cagtgtctcc tccaggagg atgtgggatt tgatacgtgg     360
gaatgacagg gtttggcaat cccatagctt ctgaattcca gggaggggag gagaaagatg     420
cgggtgaaaa cctgctttca gaggggtttc ccttggtgct ctcctcaacc aaactcacc     480
acaaattgca tgtcaagttt cccaacctcc acctagggga gcaggctctt tcaattcaga     540
gaattcagag gcatctcgag ggcattatgcc agggcaggca cagagttagg aggtgggggt     600
gggggttttt ggacagctct ggtccctctc agccccacag agcatgcaat gtggctgatg     660
ctgctggaga gctggtctct gaaaggagaa tgcattgaat tgaactagaa acagaagggc     720
agaaggacca ggaaaagaaa tgagagccaa acagagtctg agcaatgaaa ggatgtttca     780

```


gagagctgaa aacacaagct aagctaagca tcagtggact gggagagctc tgcaaaata 839

<210> 178
 <211> 646
 <212> DNA
 <213> Homo sapien

<400> 178
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 gctgcagagg caggatgggc ccaggccct caagccatt cttctcttg ctcctgttcc 120
 atctcggcag tgcttcctcc agggaggatg tgggatttga tacgtgggaa tgacagggtt 180
 tggcaatccc atagcttctg aattccaggg aggggaggag aaagatgagg gtgaaaacct 240
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 cagctctggt cccctccagc cccacagagc atgcaatgtg gctgatgctg ctggagagct 480
 ggtctctgaa aggagaatgc atgaatctga actagaaaca gaagggcaga aggaccagga 540
 aaagaaatga gagccaaaca gactctgagc aatgaaagga tgtttcagag agctgaaaac 600
 acaagctaag ctaagcatca gtggactggg agagctctgc aaaata 646

<210> 179
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 179
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 gccaaagtga acagggaccc atccacatcc cccttagaga tcaaacaatt gtgtctcgaa 120
 gcagcaaacc tccttctcag ccatcacctg ctgggcatgt tctgggtgag cctggggaag 180
 atgatatgtg ccccatcgta aagtgaaga actgcatctc agggctccac agagcaccca 240
 gagtccagtg ctgcagaggc aggatggccc agggccctca agccattct tctcttggct 300
 cctgttccat ctcggcagtg cttcctccag ggaggatgtg ggatttgata cgtgggaatg 360
 acagggtttg gcaatcccat agcttctgaa ttocaggag gggaggagaa agatgcgggt 420
 gaaaacctgc tttcagaggg ttttccttg gctgcctcct caaccaaact caccacaaa 480
 ttgcatgtca agtttccaa cctccaccta ggggagcagg c 521

<210> 180
 <211> 215
 <212> DNA

203

<213> Homo sapien

<400> 180

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aaaagtgatt acatggggtt attcttggtg gagaaggtgt tgtaaccacg ggggcaaagc      60
cctaatacta tggattagct acaagatccc agtaatagct ttggattcaa aatcttcctt      120
tgcgaggctc ttctcactaa tgcagtttca tttgggctaa aattcagggg atctgagttc      180
ctgttcgact gtgcaattta ccagctacat ggacc                                215

```

<210> 181

<211> 215

<212> DNA

<213> Homo sapien

<400> 181

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aaaagtgatt acatggggtt attcttggtg gagaatgtgt tgtaaccaca tgggcaaagc      60
cctaatacta tggattagct acaagatccc agtaatagct ttggattcaa aatcttcctt      120
tgcgaggctc ttctcactaa tgcagtttca tttggtctaa aattcagggg atctgagttc      180
ctgttcgact gtgcaattta ccagctacat ggacc                                215

```

<210> 182

<211> 858

<212> DNA

<213> Homo sapien

<400> 182

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ttagaaaaag tgtctcacat tcccgttcag gggcccaagc atctgcctcc tctcctgcac      60
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tgctgctttc tgggcagtgg cctagaactt caaggctgat gagcatatgc agaaggcagg      180
aggacacagt ctggctggct tgggcctcac tagctgacag aggggctgcc cagcctgacc      240
acaggggttt catggcaggg actccagacc actcactcat cctatctgac ttcacacacc      300
acctggcttc tgetcagagc tgccattgtg ccttcctga catgagtga gctgggacac      360
acaccagggg aaggctcttg tctcctgcca agtccacagg ggagaaagcg ttacctccag      420
ggaaacagag gcagccgtgc tctgtcacta ccaatttgta caaggcacag ggcctaattg      480
ttgactttct acagcaagtc tctgtgtga gaccaggacc tcttcccagc attctaaatg      540
caagacatct caacagccca gcatgtcaga gtggcatccc gtaggatgtc tgctttctct      600
catcagtcct ggagtgcac ctcagagaat gcctgtgagc agcatccgac agagactacc      660
aaciaactgg cccaggcatc tggcaccaga gaaaaatgaa ctcccagtag acagttccac      720
cacgtgacat tttcatgatt gacagccctc tcccactttc cctagcctgg cttacatgtt      780
gagaaggtag gattcccat tacgagagga ggtggtctct gagcaaccac agtgatgttt      840

```

204

ccattctgga gacttacc

858

<210> 183

<211> 857

<212> DNA

<213> Homo sapien

<400> 183

| | |
|--|-----|
| ttagaaaaag tgtctcacat tcccgttcag gggcccagca tctgctcct ctcctgcaca | 60 |
| gagggctctgg gcttctcggg gcctgtaagt tggctaagcc cctcatcgga ccactggtct | 120 |
| gctgctttct gggcagtggc ctagaacttc aaggctgatg agcatatgca gaaggcagga | 180 |
| ggacacagtc tggctggctt gggcctcact agctgacaga ggggctgcc agcctgacca | 240 |
| caggggtttc atggcagga ctccagacca ctactcatc ctatctgact tcacacacca | 300 |
| cctggcttct gctcagagct gccattgtgc cttccctgac atgagtgcag ctgggacaca | 360 |
| caccagggaa aggtcttctg ctctgccaa gtccacaggg gagaaagcgt tacctccagg | 420 |
| gaaacagagg cagccgtgct ctgtcactac caatttgtac aaggcacagg gcctaattgt | 480 |
| tgactttcta cagcaagtct cctgtgtgag accaggacct cttcccagca ttctaaatgc | 540 |
| aagacatctc aacagcccag catgtcagag tggcatcccg taggatgtct gctttctctc | 600 |
| atcagtcttg gagtcgcacc tcagagaatg cctgtgagca gcatccgaca gagactacca | 660 |
| acaaactggc ccaggcatct ggcaccagag aaaaatgaac tcccagtaga cagttccacc | 720 |
| acgtgacatt ttcatgattg acagccctct cccactttcc ctagcctggc ttacatgttg | 780 |
| agaaggtagg attccccatt acgagaggag gtggctctctg agcaaccaca gtgatgtttc | 840 |
| cattctggag acttact | 857 |

<210> 184

<211> 392

<212> DNA

<213> Homo sapien

<400> 184

| | |
|--|-----|
| ggggattggg gggcagtcag aaacggggca ggctcccagg ctctgctctt gtgacggagc | 60 |
| acctctgcaa gagaagacga cacgggtctc atgtgctcca aggggtgggag gtcacagagg | 120 |
| agctggcaga gaagagtccc aaaaatatcc aaggcgtgtc tcgatgagac catctgaagg | 180 |
| cggcgctttg ctccctacgc cggggacagc gcccgcgaac actgtggcct ccacagcctg | 240 |
| acaaagctgt gagctgcgtg ggaagccatc ggccttggcc atggccatgc acctgcagcc | 300 |
| caaatggaga cagtttctcc tctgcatctc atcacagatg ttaccctggg tcttgcactg | 360 |
| attcaaatac atctatggct tttattttat tt | 392 |

205

<210> 185
 <211> 392
 <212> DNA
 <213> Homo sapien

<400> 185
 ggggattggg gggcagtcag aaacggggca ggctcccagg ctctgctctt gtgacggagc 60
 acctctgcaa gagaagacga cacgggtctc atgtgctcca aggggtgggag gtcacagagg 120
 agctggcaga gaagagtccc aaaaatatcc aaggcgtgtc tcgatgagac catctgaagg 180
 cggcgctttg ctccctacgc cggggacagc gcccgccaac actgtggcct ccacagcctg 240
 acaaagctgt gagctgcgtg ggaagccatc ggccttggcc atggccatgc acctgcagcc 300
 caaatggaga cagttttctcc tctgcatctc atcacagatg ttaccctggg tcttgcactg 360
 attcaaatac atctatggct tttattttat tt 392

<210> 186
 <211> 632
 <212> DNA
 <213> Homo sapien

<400> 186
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 tcaacaattt aacaaaaatt aacgatgtaa ttccaatcaa atctaaacct ctagccacaa 120
 aaccttaaat tcaagggtgct gatcttaatc taaaaaacct catgtgggtt gggttctggt 180
 taccttagag atttgactct aagcacccaa aggcatttaa gattagatga aatacttggc 240
 cgatggttca ctactgaaac ctgatgaact ggaatcctct gattttaatt gcctttgggt 300
 gcttagagtc aaatctctaa ggtaaccaga acccaaacca catgagggtt ttagattaa 360
 gatcagcacc ttgaatttaa ggttttgtgg ctagagggtt agatttgatt ggaattacat 420
 cgtaattttt tgttaaattg ttgaataagc aacttcccaa gccttgtgtg tagaagctag 480
 attaaaagtc aagtttctac ttaaccagaa tctctgtttt gagtttttaa attcaactgg 540
 tgatgtctaa atcttaagga tattgtaagt tccttaacta gtctgttcca ttttctgag 600
 ttttcacatc acctctctac ctcttgtgta ga 632

<210> 187
 <211> 457
 <212> DNA
 <213> Homo sapien

<400> 187
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 tcatcagggt tcagtagtga accatcggcc aagtatttca tctaatttta attgcctttg 120
 ggtgcttaga gtcaaactct taaggtaacc agaaccctaaa ccacatgagg ttttttagat 180

206

taagatcagc acottgaatt taaggttttg tggctagagg tttagatttg attggaatta 240
catcgtaaatt ttttgtaaata ttgttgaata agcaacttcc caagccttgt gtgtagaagc 300
tagattaaaa gtcaagtttc tacttaacca gaatctctgt tttgagtttt taaattcaac 360
tggatgatgc taaatcttaa ggatattgta agttccttaa ctagtctgtt ccattttcct 420
gagttttcac atcacctctc tacctcttgt gtagatt 457

<210> 188
<211> 680
<212> DNA
<213> Homo sapien

<400> 188
ggctacatta cacggtgaat cccgtcttac taaaaagaca aaaaattagc tgggtgtggt 60
tgcaggcgcc tgcagtcacca gctactcagg aggttgaggc aggagaatcg ctttaaccca 120
ggaggtagag cttgcagtga cccaagattg tccaatgca ctgcacgcct gggtagacaga 180
actgagattg tgtgtactga aattacaaac aatcaaaca gaccgcgaga aatgggttgt 240
caccctatct gaaaagagac acacaaaatc agaggattcc agttcatcag gtttcagtag 300
tgaaccatcg gccaaagtatt tcatctaate ttaattgcct ttgggtgctt agagtcaaatt 360
ctctaaggta accagaaccc aaaccacatg aggtttttta gattaagatc agcaccttga 420
atttaagggt ttgtggctag aggttttagat ttgattggaa ttacatcggt aatttttgtt 480
aaattgttga ataagcaact tccaagcct tgtgtgtaga agctagatta aaagtcaagt 540
ttctacttaa ccagaatctc tgttttgagt ttttaaattc aactgggtgat gtctaaatct 600
taaggatatt gtaagttcct taactagtct gttccatttt cctgagtttt cacatcacct 660
ctctacctct tgtgtagatt 680

<210> 189
<211> 605
<212> DNA
<213> Homo sapien

<400> 189
gcctgtaatc ccagctgctt gggaggctga ggcaggagaa tcgcttgaac ccaggaggta 60
gagcttgtag tgagccaaga ttgtgccaat gcactgcagc ctgggtgaca gactgagact 120
gtgtctgaaa aacaaacaaa caaacaaaac ccagaatgg ttggtcaccc tatctgaaaa 180
gagacacaca aaatcagagg attccagttc atcaggtttc agtagtgaac catcggccaa 240
gtatttcac taaatctaat tgcctttggg tgcttagagt caaatctcta aggttaaccag 300
aaccctaaacc acatgagggt ttttagatta agatcagcac cttgaattta aggttttgtg 360

207

| | |
|--|-----|
| gctagagggtt tagatttgat tggaattaca tcgttaattt ttgttaaatt gttgaataag | 420 |
| caacttccca agccttggtg gtagaagcta gattaaaagt caagtttcta ctttaaccaga | 480 |
| atctctgttt tgagttttta aattcaactg gtgatgtcta aatcttaagg atattgtaag | 540 |
| ttccttaact agtctgttcc attttcctga gttttcacat cacctctcta cctcttggtg | 600 |
| agatt | 605 |

<210> 190
 <211> 445
 <212> DNA
 <213> Homo sapien

| | |
|--|-----|
| <400> 190 | |
| agatttgact ctaagcacc aaaggcatta agattagatg aaatacttgg ccgatgggtc | 60 |
| actactgaaa cctgatgaac tggaatcctc tgattttaat tgcctttggg tgccttagagt | 120 |
| caaactctcta aggtaaccag aacccaaacc acatgagggt ttttagatta agatcagcac | 180 |
| cttgaattta aggttttgtg gctagagggt tagatttgat tggaattaca tcgttaattt | 240 |
| ttgttaaatt gttgaataag caacttccca agccttggtg gtagaagcta gattaaaagt | 300 |
| caagtttcta ctttaaccaga atctctgttt tgagttttta aattcaactg gtgatgtcta | 360 |
| aatcttaagg atattgtaag ttccttaact agtctgttcc attttcctga gttttcacat | 420 |
| cacctctcta cctcttggtg agatt | 445 |

<210> 191
 <211> 578
 <212> DNA
 <213> Homo sapien

| | |
|--|-----|
| <400> 191 | |
| aagctccatt cctgaaggct gggacagcat taggggacag gagtaagggtg acaaagcaga | 60 |
| aactcttccc caagagctgc ctggcacgtc aagatgcaaa agcctaaaac ctttgaccaa | 120 |
| gacactgggc agaggtttta ggcttttgca tcttgacgtg ggagatagag agcctgtgag | 180 |
| ggagaggcac cagagacgga gacgctggca ggtgcttga tcaatagctt tcaggaatca | 240 |
| ggttgacagc tcagatcaaa agctccattc ctgaaggctg ggacagcatt aggggacagg | 300 |
| agtaagggtga caaagcagaa actcttcccc aagagctgcc tggcaccctt catttcagac | 360 |
| tccgaagaaa aagaaggctc ccttctagtg ggggtgaagc cccagggtca cagcagttct | 420 |
| cagcatggtg ccccagcaga ctggcctggg tatcgggaga cacactgcaa tgatctgtca | 480 |
| cttaaaacac ttgtggagtg acagtgttg aaaactgctt acctttttta aaaatgtttt | 540 |
| aacttttaaa taactaagta aataaggctg gagcacac | 578 |

<210> 192
 <211> 744
 <212> DNA
 <213> Homo sapien

<400> 192
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 agtagagatg gggtttacca tgttgggcag gctggctctg aactcccgac ctcagggtgat 120
 ccgccagcct cggcttccca aagtgtctggg attacaggca ggagccactg tgtccagcct 180
 tatttactta gttatttaaa agttaaaaca ttttttaaaa aggtaagcag ttttccaaca 240
 ctgtcactcc acaagtgttt taagtgcag atcattgcag tgtgtctccc gatacccagg 300
 ccagtctgct ggggcaccat gctgagaact gctgtgaacc tggggcttca accccactag 360
 aaggggacct tctttttctt cggagtctga aatgaagggt gccaggcagc tcttggggaa 420
 gagtttctgc tttgtcacct tactcctgtc ccctaagtct gtcccagcct tcaggaatgg 480
 agcttttgat ctgagtctgc aacctgattc ctgaaagcta ttgatcaagc accctgccag 540
 cgtctccgtc tctgggtgct ctccctcaca ggctctctat ctcccacgtc aagatgcaaa 600
 agcctaaaac ctctgccag tgtcttggtc aaagggttta ggcttttgca tcttgacgtg 660
 ccaggcagct cttggggaag agtttctgct ttgtcacctt actcctgtcc cctaagtctg 720
 tcccagcctt caggaatgga gctt 744

<210> 193
 <211> 742
 <212> DNA
 <213> Homo sapien

<400> 193
 aggacctgaa gctgggatta caagtgtccg ccagtacact tggctaattt ttgtagtttt 60
 agtagagatg gggtttacca tgttgggcag gctggctctg aactcccgac ctcagggtgat 120
 ccgccagcct cggcttccca aagtgtctggg attacaggca ggagccactg tgtccagcct 180
 atttacttag ttatttataaa gtaaaacatt ttttataaaag gtaagcagtt ttccaacact 240
 gtcactccac aagtgtttta agtgacagat cattgcagtg tgtctcccga taccagggcc 300
 agtctgctgg ggcaccatgc tgagaactgc tgtgaacctg gggcttcaac ccactagaa 360
 ggggaccttc tttttcttcg gagtctgaaa tgaagggtgc caggcagctc ttggggaaga 420
 gtttctgctt tgtcacotta ctctgtccc ctaagtctgt ccagccttc aggaatggag 480
 cttttgatct gagtctgcaa cctgattcct gaaagctatt gatcaagcac cctgccagcg 540
 tctcogtctc tgggtgcctct ccctcacagg ctctctatct cccacgtcaa gatgcaaaag 600
 cctaaaacct ctgccagtg tcttgggtcaa aggttttagg cttttgcatc ttgacgtgcc 660

209

aggcagctct tggggaagag tttctgcttt gtcaccttac tcctgtcccc taatgctgtc 720

ccagccttca ggaatggagc tt 742

<210> 194
 <211> 350
 <212> DNA
 <213> Homo sapien

<400> 194
 cttggaagtt gtacttttgg ataaatatgc cttcttggta aagatcaagg gtaacagggg 60
 agggaaagat tccatgtagg actatgggga ggggagaatg catttgaagc tctctctaag 120
 acatcagcag ctcccttggg caaagagaaa ctgccccgac agaaagaaac atttttgggt 180
 attagttaaa cattgcctga atatttggat cttgcttttt tctctcctcc tccaagaata 240
 agttttaatg gcctggggtt acagatccac acgggaccta aggagggagc ggttgatttg 300
 actttcactt gatttactaa agcaattgaa tttgtcgggg gaaatttgat 350

<210> 195
 <211> 350
 <212> DNA
 <213> Homo sapien

<400> 195
 cttggaagtt gtacttttgg ataaatatgc cttcttggta aagatcaagg gtaacagggg 60
 agggaaagat tccatgtagg actatgggga ggggagaatg catttgaagc tctctctaag 120
 acatcagcag ctcccttggg caaagagaaa ctgccccgac agaaagaaac atttttgggt 180
 attagttaaa cattgcctga atatttggat cttgcttttt tctctcctcc tccaagaaca 240
 agtttttagtg gcctggggtt agagagccac acgggaccta aggagggagg ggttgatttg 300
 actttcactt gatttactaa agcaattgag tttgtcgggg gaaatgtgat 350

<210> 196
 <211> 553
 <212> DNA
 <213> Homo sapien

<400> 196
 aaaagttaa aacaacctga tgaccataa gtaggaactg gttaaataaa ttgtatcttt 60
 caccaggaga tcctatgcat ctttaaataa gaatgaagaa gtcgttttgt acatacacia 120
 atgtggaata ttatgtagct gtgttaaatt taaaaatca aatgcagaag atctctgtgt 180
 actaatagga aaatatatct tggacttttc cagtgaagaa agcaaagtgc attggccgtg 240
 ctagctcctg cttgactttc taatccctgg ggcccaatgc tgtacttggg tttggttttg 300
 tttattttgt tttcttcttc tgtcctttcc aaacacgcac acttattggg tctattgttt 360

210

gcctaaccct ttgatactat acccagcagc tctcatcttt ccacctattc agacctgtgg 420
 ctgcccctga ccttggtacc tatattgcc aagacttctcc atgctgcctt cacttacagc 480
 acaatatgga ctatcctggc atgctagtgt cttttcttct aagctacatc ttgggctctt 540
 agaaagaaat gca 553

<210> 197
 <211> 554
 <212> DNA
 <213> Homo sapien

<400> 197
 aaaagtttta aaacaacctg atgaccata agtaggaact ggtaaataa attgtatctt 60
 tcactaggag atcctatgca tttttaata agaatgaaga agtcgttttg tacatacaca 120
 aatgtggaat attatgtagc tgtgttaaata tttaaaaatc aaatgcagaa gatctctgtg 180
 tactaatagg aaaatatatt ttggactttt ccagtgaag aagcaaagtg cattggccgt 240
 gctagctcct gcttgacttt ctaatccctg gggcccaatg ctgtacttgg ttttggtttt 300
 gtttatcttg ttttcttctt ctgtcctttc caaacacgca cacttattgg ttctattgtt 360
 tgcctaacc tttgatacta taccagcag ctctcatctt tccacctatt cagacctgtg 420
 gctgcccctg accttggtac ctatattgcc aagacttctc catgctgcct tcacttacag 480
 cacaatatgg actatcctgg catgctagtg tctttcttct taagcttcat cttgggctct 540
 tagaaagaaa tgca 554

<210> 198
 <211> 106
 <212> DNA
 <213> Homo sapien

<400> 198
 caagactctg tctcaaaaaa agaaaaaag acccataagg cttttagaag aaaatacagg 60
 agaaaatctt tggaacataa gactacgtga agaggctggg tgtggt 106

<210> 199
 <211> 106
 <212> DNA
 <213> Homo sapien

<400> 199
 caagactctg tctcaaaaaa agaaaaaag acccataagg cttttagaag aaaatacagg 60
 agaaaatctt tggaacataa gactacgtga agaggctggg tgtggt 106

<210> 200
 <211> 104
 <212> DNA

211

<213> Homo sapien

<400> 200

caagactctg tctcaaaaaa agaaaaaaag acccataagg cttttagaag aaaatcagga 60

gaaaatcttt ggaacataag actcgtgaag aggctgggtg tggt 104

<210> 201

<211> 719

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (76)..(155)

<223> n=a,c,g or t

<220>

<221> misc_feature

<222> (620)..(620)

<223> n=a,c,g or t

<400> 201

ttgttcccaa aaaatgttta caatggacat gtattttatg tgaacttttt aaaaagttac 60

ttctattgta agaaannnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 120

nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnagaag aaaacttgat agccttgatg 180

gatataaaaa gaaaacttat ctaattataa gacatcccct attattgaat agaaagtctt 240

agaattataa atacagcaat tctgtcttca gttagtctat aagtgtaatg gttatattag 300

aacagcccaa gtttactgca gttacaaatt aaccctgaaa tccccctgtc tgacgctgag 360

tttcttgctc agtcatgccg cagttccatt gtgggctgat aggagtctct gtccgcatag 420

aggcttagac ccattcaggg gtctagactc tctgaggetg tgccatcttg gagttacatc 480

atctgaaaga agtaccacgc tcagaggctg tggcaggaaa agaaggaggg gagtcaaaat 540

ccagcaacta aatgttttgg cctggaaaca tcacatgaca cttggctatt ggccagacta 600

atcacataac cccacctgan tgcagggagg caaggaactt cagtctttcg tacgtgcagg 660

aatcagaaaa gatccagata ctggtgaata ctcgtgggtt tcaataaaaa taccattga 719

<210> 202

<211> 449

<212> DNA

<213> Homo sapien

<400> 202

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gtcttagaat tataaataca gcaattctgt cttcagttag tctataagtg taatggttat 120

212

attagaacag cccaagttaa ctgcagttac aaattaaccc tgaaatcccc ctgtctgacg 180
 ctgagtttct tgctcagtca tgccgcagtt ccattgtggg ctgataggag tctctgtccg 240
 catagaggtc tagaccatt caggggtcta gactctctga ggctgtgcca tcttgagtt 300
 acatcatctg aaagaagtac cacgctcaga ggctgtggca ggaaaagaag gaggggagtc 360
 aaaatccagc aactaaatgt tttggcctgg aaacatcaca tgacacttgg ctattggcca 420
 gactaatcac ataaccacac ctgaatgca 449

<210> 203
 <211> 752
 <212> DNA
 <213> Homo sapien

<400> 203
 gcttcagaa ggccatgggc ggagcatgg gccctcctgg gaaagtgtga aaggccaagg 60
 ccccaaaaca ccacaggggtg tagcagttag ggctgggtca ggtgagaaca gcggcatgaa 120
 gttgccaac ttgggggttg aaatcacagt ttgggagcgg ctccaatcca aaccatgaca 180
 ccatacggga tctttcagcc acttgaggg gcggagctgg cggcgggatt gacctgggat 240
 tggggatttg cgggggtggg agctggtggg gtccggcgga aaggggagga cgtgaacttg 300
 ggcgggttgc cctggagagg cctgtagatg ctgggcaggt gggaaggcag gtttccaggt 360
 ggcagcgggt ggagaggagg tgggggactt gtggtcagag agcgccctg gcggggattt 420
 ggggatcagc atgcaggaag ctctggtgat gacaccacag ggcgtgtgt gaaacggatt 480
 caggctgcca agcggtattc actgtggaga gattgtcatc accagagccg tgtctaaagg 540
 atttagccag ggctggatac ggaaaacaga atggaagggg gctttgggag accagccac 600
 ctcaacaaga agagctgaga gcctagattt gggccagcgg gggtagtctc tggacggagg 660
 gcggcacggg gctggaggag gagcgtttta tgatgcggcc gtgggtgctg gccttggtg 720
 gggcttgtgg cgactgggtg ccgtgacgtg gg 752

<210> 204
 <211> 1024
 <212> DNA
 <213> Homo sapien

<400> 204
 cctgagtcac cggcgtgtg gtccccgcc ccaggcttgt ggcctcctg tctccagtc 60
 gtgctcgggt ctgctgcca gccccgcgc ctccgcgcgc ttcttgccc ttgcggttga 120
 cggccgagat gaaggagatc gccagcatct cccgggcgta cggctcctc ttgggggccc 180
 acgaaccctg tgtgggagac aggtcaggat gcggggggcg tcccggactc ggcccctctg 240
 ccgacccgt cttctatctc cggctcctacc tctccacgtc acggcaccac gtccgacaa 300

213

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gccccagcca aggccagcac ccacggccgc atcataaaac gtcctcctc cagccccgtg      360
ccgccctccg tccagagact acccccgtg gcccaaactc aggcctctcag ctctttcttg      420
tgagggtggg tggtctcca aagccccctt ccattctgtt ttccgtatcc agccctggct      480
aaatccttta gacacggctc tggatgatgac aatctctcca cagtgaataa cgcttggcag      540
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caacttcatt ccgctgttct cacctgaacc agccctcact gctacacct gtggtgtttt      960
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<210> 205

<211> 2981

<212> DNA

<213> Homo sapien

<400> 205

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| | |
|--|------|
| aagccaagca cgtccctgcc tctgctgtgg tctccagtgc catgaactca gccctgtcc | 900 |
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| gcctgccaaa ccgcataccc agcctgcgga tgctccggag cttcttcacc gacgggtcct | 1140 |
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| cctgcctcgt ggacatctcc tacagcgaga ccaagaggag gcacgtgttc cggctgacca | 1500 |
| ccgctgactt ctgtgaatat ctctttcagg ctgaggaccg ggatgacatg ctgggctgga | 1560 |
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| ctgcagcccc caaaaccccc tggggcatca acatcatcaa gaaaaataag aaggccgctc | 1860 |
| cgagggcggt tggggtcagg ctggaggagt gccagccagc cagggagaa cagcgctcc | 1920 |
| ccttaatcgt ggctgcatgc tgtcgcatgt tggaggcacg agggctggag tccacaggca | 1980 |
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| acctgttgga gatttaaagg attctaccac ctgtagttca gccaaagtcca agggttcgtg | 2640 |

215

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<210> 206

<211> 608

<212> DNA

<213> Homo sapien

<400> 206

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 tttactgat gacaaataca acgacttcat cgaggccaac cgatttgagg acgcgcggga 480
 gcgaatgagg acgctgcgga agctgatccg ggatctccca ggacactact atgaaacgct 540
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<210> 207

<211> 752

<212> DNA

<213> Homo sapien

<400> 207

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 gttgcccac ttgggggttg aaatcacagt ttgggagcgg ctccaatcca aaccatgaca 180
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216

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<210> 208
<211> 991
<212> DNA
<213> Homo sapien

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<210> 209
<211> 2958
<212> DNA
<213> Homo 'sapien

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<400> 209

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217

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| ggaggagggtg gctgcccccc gccctggcc ctgctccacc tcccaggatg ctttgagcca | 180 |
| gctgggccag gagggctggc accgagctcg ctacagatgac tacttgagcc gggccaccgc | 240 |
| ttctgccag gactggggc caggggcact ggtgtcacc cgctttgagc ggtgtggctg | 300 |
| ggcttcccag cgttcgtctg ccgcacccc cgctgccc actcgggacc tgccagggcc | 360 |
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| gagctacagc ccatcattcc agcagccgga ccggcctcct ccatgcgctc tccttcggg | 480 |
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| cagaggcctc cgagccacc agggttgtac ggccggaacc cagcaccgcg gccctggagc | 600 |
| ctcctgcgga ggatgcggc gatgagggtg tcctgaggca gaagccccg acgggcccga | 660 |
| aggttcagct gacccccga agacagatga acctggatt tggtgacgag tcccagagc | 720 |
| cagaggccag tgggcgagg gaacgcctgg gcaggaagg gggcccttg gccaccaccg | 780 |
| aagactctct ggcttccatc ccctttattg atgagccac cagcccagc attgacctc | 840 |
| aagccaagca cgtccctgcc tctgctgtg tctccagtgc catgaactca gccctgtcc | 900 |
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| gctccaagtc ctgcgatgat ggactcaaca ccttcgcga cgaggcccg gttctgcggc | 1080 |
| gcctgcaaaa ccgcataccc agcctgcgga tgctccggag cttcttcacc gacgggtcct | 1140 |
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| acctctcaga tgcgacctc agcgatatca ggagagaagg ctggttgat tataagcaga | 1260 |
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| agagtgcggc acgtggcctc aggactcagg acctgcccgc agggagcaag gatgacagt | 1800 |
| ctgcagcccc caaaacccc tggggcatca acatcatcaa gaaaaataag aaggccgctc | 1860 |

218

cgagggcggtt tggggtcagg ctggaggagt gccagccagc cacggagaac cagcgcgtcc 1920
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<211> 4624

<212> DNA

<213> Homo sapien

<400> 210

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| | | | | | | |
|------------|------------|------------|-------------|------------|-------------|------|
| actcaccctt | tggggggctg | cctaccttca | acctggccca | gtcccctgcg | tcattccac | 540 |
| cagaggcctc | cgagccaccc | agggttgtac | ggccggaacc | cagcaccg | gccctggagc | 600 |
| ctcctgcgga | ggatcgcggc | gatgaggtag | tcctgaggca | gaagcccccg | acgggcccga | 660 |
| aggttcagct | gacccccgca | agacagatga | accttggatt | tggtgacgag | ccccagagc | 720 |
| cagaggccag | tgggcgaggg | gaacgcctgg | gcagggaaggt | ggcccctttg | gccaccaccg | 780 |
| aagactctct | ggcttccatc | ccctttattg | atgagccca | cagccccagc | attgacctcc | 840 |
| aagccaagca | cgtccctgcc | tctgctgtgg | tctccagtgc | catgaactca | gcccctgtcc | 900 |
| tgggcaccag | cccatcttcc | cgcaccttca | ctttcacctc | cggacgcat | tactcgagg | 960 |
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| cgagggcgtt | tggggtcagg | ctggaggagt | gccagccagc | cacggagaac | cagcgcgctc | 1920 |
| ccttaatcgt | ggctgcatgc | tgtcgcattg | tggaggcacg | agggctggag | tccacaggca | 1980 |
| tttaccgagt | gcccggcaac | aatgcagtag | tgtccagcct | acaggagcag | ctcaaccgcg | 2040 |
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220

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221

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226

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| ccaggcccca | accccgctctg | gcctgcaggg | cctggatgac | ctcgggtaca | tcggctaccg | 420 |
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228

| | | | | | | |
|-------------|------------|-------------|------------|------------|------------|------|
| ttctcaccaa | gaaggggaag | aaagcgggca | gcggcctgcg | ccagtggaag | cgggtgtacg | 1320 |
| ccgcgctgcg | ggcgcgctcg | ctctcgctga | gcaaggagcg | gcgggagccc | gggccggcg | 1380 |
| cggcgggggc | tgcggggggc | ggcgcagggtg | aggacgaggc | ggcgcccgtc | tgcctcggct | 1440 |
| cctgcctcgt | ggacatctcc | tacagcgaga | ccaagaggag | gcacgtgttc | cggctgacca | 1500 |
| ccgctgactt | ctgtgaatat | ctctttcagg | ctgaggaccg | ggatgacatg | ctgggctgga | 1560 |
| tcagagcgat | ccgggagaac | agcagggccg | agggcgagga | ccccggctgt | gccaaccaag | 1620 |
| ctctgatcag | caagaagctt | aatgattatc | gcaaagttag | ccatagctct | gggcccaaag | 1680 |
| ctgattcctc | cccaaaggc | tctcgcgcc | tggggggcct | caagtctgag | ttcctcaagc | 1740 |
| agagtgcggc | acgtggcctc | aggactcagg | acctgcccgc | agggagcaag | gatgacagt | 1800 |
| ctgcagcccc | caaaaccccc | tggggcatca | acatcatcaa | gaaaaataag | aaggccgctc | 1860 |
| cgagggcggt | tggggtcagg | ctggaggagt | gccagccagc | cacggagaac | cagcgcgctc | 1920 |
| ccttaatcgt | ggctgcatgc | tgtcgcatgt | tggaggcacg | agggctggag | tccacaggca | 1980 |
| tttaccgagt | gcccggcaac | aatgcagtgg | tgtccagcct | acaggagcag | ctcaaccgcg | 2040 |
| ggcctgggtga | catcaacctg | caggatgagg | tgggtgaagc | tggggggctc | gtggaagggg | 2100 |
| ggctgagatg | gtgtgtgggt | ggtgctccgc | ttggagagtt | ctgtggtcta | ttgtgttgca | 2160 |
| tgcattgtgc | cctatgacat | gcccggcatt | ggtccagaac | accaagatgg | gcaagatggg | 2220 |
| acctgcccc | gctggccagc | ccggggatgg | gcatcacccc | aggtgaagc | tgaccaagta | 2280 |
| aatgcagtca | tggcctgggg | agctctgagg | cagaggctca | cagatggcag | ttttgtccga | 2340 |
| gtgttttagga | tgagtagagt | tcaccaaagg | ccggtgaaag | ccaggtgagg | gcattccagg | 2400 |
| cagcagaatg | gcctgctcaa | tggtgtagac | gcggaaagt | | | 2439 |

<210> 216

<211> 889

<212> DNA

<213> Homo sapien

<400> 216

| | | | | | | |
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| ctcccagcag | ggcccttggc | cgggagagca | ggggaaggcg | ctgccccac | ctctctaaag | 60 |
| agtctccgct | gtgttctaga | caaatacaac | gacttcacg | aggccaaccg | cattgaggac | 120 |
| gcgcgggagc | gaatgaggac | gctgcggaag | ctgatccggg | atctcccagg | acactactat | 180 |
| gaaacgctca | aattccttgt | gggccatctc | aagaccatcg | ctgaccactc | tgagaaaaac | 240 |
| aagatggaac | cccggaaacct | ggccctggtc | tttgggcca | cactgggtgag | gacgtctgag | 300 |
| gacaacatga | cagacatggg | gaccacatg | cctgaccgct | acaagatcgt | ggagacactg | 360 |
| atccagcact | cagactgggt | cttcagttag | gaagaggaca | agggagagag | aaccctgtg | 420 |

229

ggcgacaagg agcctcaggc agtgcccaac attgagtacc tcctgcccac cattggcagg 480
 acagtgcccc ctggcgaccc ggggtcagat totaccacct gtagttcagc caagtccaag 540
 ggttcgtggg cccccaagaa ggagccgtac gcccgggaga tgctggcgat ctcttcatc 600
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 gacgacgact cggagcagga ggcgcaaac cctggggcgg gggccacagc gccggggact 720
 caggagcggc cgccggggag ccgatgcccg gcgcggcggc ccgatgcccc gcgcggcgc 780
 caccgcggcc cccggacccg gcagtcccc ggcggcgcgg gaggggcccgc cggccgcggc 840
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<210> 217

<211> 2106

<212> DNA

<213> Homo sapien

<400> 217

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 ggaggagggtg gctgcccccc gcccggtggc ctgctccacc tcccaggatg ctttgagcca 180
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 ccaggcccca acccgtctg gcctgcagg cctggatgac ctgggtaca tcggctaccg 420
 gagctacagc ccattattcc agcgaccgga ccggcctcct ccattgcgctc tccttccggg 480
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 aggttcagct gacccccgca agacagatga accttgatt tggtagcag tcccagagc 720
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 gctccaagtc ctgcgatgat ggactcaaca ccttccgca cgaggccgg gttctgcggc 1080
 gcctgcaaaa ccgcataccc agcctgcgga tgctccggag cttcttacc gacgggtcct 1140

230

| | | | | | | |
|-------------|------------|------------|------------|-------------|-------------|------|
| tggaatagctg | gggcacctct | gaagatgctg | acgctccttc | taagcgacac | tcaacctctg | 1200 |
| acctctcaga | tgcgaccttc | agcgatatca | ggagagaagg | ctggttgat | tataagcaga | 1260 |
| ttctcaccaa | gaaggggaag | aaagcgggca | gcggcctgcg | ccagtgggaag | cggtgtacg | 1320 |
| ccgcgctgcg | ggcgcgctcg | ctctcgctga | gcaaggagcg | gcgggagccc | ggccggcg | 1380 |
| cgccgggggc | tgcggcgccc | ggcgaggtg | aggacgaggc | ggcgcccgtc | tgcacggct | 1440 |
| cctgcctcgt | ggacatctcc | tacagcgaga | ccaagaggag | gcacgtgttc | cggtgacca | 1500 |
| ccgctgactt | ctgtgaatat | ctctttcagg | ctgaggaccg | ggatgacatg | ctgggctgga | 1560 |
| tcagagcgat | ccgggagaac | agcagggccg | agggcgaggt | gagggcccg | ccagcccg | 1620 |
| agccacagag | ggcgggcg | gtggcctctc | accggctgtg | gacctgggat | gcccgcctctg | 1680 |
| agcctcactt | ccctctgcta | gaaagggggg | ctgacaggag | tgcacctcgt | gattgtgtcc | 1740 |
| cccaaggttt | cggggtgagg | aggtgcaca | ggcagggtc | acgggggtaa | gagtgaagga | 1800 |
| agtactgggg | gttcgggaga | actaaggggc | tgggtgcctt | gggcatgaag | taggggtctg | 1860 |
| tgccccctcc | acactccatc | agccccact | tatgttcttc | agcacagctg | tagccaatga | 1920 |
| gaacagttat | gcaggagccc | cagagcttcc | ggcatgcatg | tgagagctgc | acagttacat | 1980 |
| gtacacatga | catgtatttg | cagacactat | atgcacacag | agagatacac | acatgcatgt | 2040 |
| ccatggccag | cacgcgatgc | acacagagag | acatgtgagc | acacgaacac | agacagtga | 2100 |
| gtcccc | | | | | | 2106 |

<210> 218

<211> 912

<212> DNA

<213> Homo sapien

<400> 218

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| ctcccagcag | ggcccttggc | cgggagagca | ggggaaggcg | ctgccccac | ctctctaaag | 60 |
| agtctccgct | gtgttctaga | caaatacaac | gacttcatcg | aggccaaccg | cattgaggac | 120 |
| gcgcgggagc | gaatgaggac | gctgcggaag | ctgatccggg | atctcccagg | acactactat | 180 |
| gaaacgctca | aattccttgt | gggccatctc | aagaccatcg | ctgaccactc | tgagaaaaac | 240 |
| aagatggaac | cccgaacct | ggccctggtc | tttgggcccga | cactggtgag | gacgtctgag | 300 |
| gacaacatga | cagacatggt | gaccacatg | cctgaccgct | acaagatcgt | ggagacactg | 360 |
| atccagcact | cagactgggt | cttcagtgc | gaagaggaca | agggagagag | aaccctgtg | 420 |
| ggcgacaagg | agcctcaggc | agtgcccaac | attgagtacc | tcctgcccac | cattggcagg | 480 |
| acagtgcgcc | ctggcgaccc | ggggtcagcg | gacctgttgg | agatttaaag | gattctacca | 540 |
| cctgtagttc | agccaagtcc | aagggttcgt | gggcccccaa | gaaggagccg | tacgcccggg | 600 |

231

agatgctggc gatctccttc atctcgcccg tcaaccgcaa gcgcaagaag cggcgggagg 660
cgcgggggct gggcagcagc accgacgacg actcggagca ggaggcgcac aagcctgggg 720
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cggccgatgc cccgcgccgc cgccaccgcg gcccccgac ccggcagtcc cccggcgggc 840
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ccatggaccg ga 912

<210> 219
<211> 515
<212> DNA
<213> Homo sapien

<400> 219
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agaacagcag ggccgagggc gaggaccccg gctgtgcca ccaagctctg atcagcaaga 180
agcttaatga ttatcgcaaa gtgagccata gctctgggcc caaagctgat tcctcccca 240
aaggctctcg cggcctgggg ggctcaagt ctgagttcct caagcagagt gcggcacgtg 300
gcctcaggac tcaggacctg cccgcaggga gcaaggatga cagtgtgca gccccaaaa 360
ccccctgggg catcaacatc atcaagaaaa ataagaaggc cgctccgagg gcgtttgggg 420
tcaggctgga ggagtgccag ccagccacgg agaaccagcg cgtcccocta tcryggctgc 480
atgctatcgc attcggctctg taacctctag gtcag 515

<210> 220
<211> 680
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (398)..(398)
<223> n=a,c,g or t

<220>
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<222> (419)..(419)
<223> n=a,c,g or t

<220>
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<222> (421)..(421)
<223> n=a,c,g or t

<220>
 <221> misc_feature
 <222> (459)..(459)
 <223> n=a,c,g or t

<220>
 <221> misc_feature
 <222> (510)..(510)
 <223> n=a,c,g or t

<400> 220
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 cgtcttccct ttataagtag ctgtggggct gctgctactc tgtctcygta gtttttcctc 120
 tccaaaaaat aagaaggccg ctccgagggc gtttggggtc aggctggagg agtgccagcc 180
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<210> 221
 <211> 2836
 <212> DNA
 <213> Homo sapien

<400> 221
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 ccaggcccca acccgtctg gcctgcagg cctggatgac ctcggttaca tcggctaccg 420
 gagctacagc ccatcattcc agcgaccgga ccggcctcct ccatgcgctc tccttcggg 480

233

| | |
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| actcaccctt tggggggctg cctaccttca acctggccca gtcccctgcg tcattcccac | 540 |
| cagaggcctc cgagccaccc agggttgtac ggccggaacc cagcaccggg gccctggagc | 600 |
| ctcctgcgga ggatcgcggc gatgaggtgg tcctgaggca gaagcccccg acgggcccga | 660 |
| aggttcagct gacccccgca agacagatga accttggtatt tggtgacgag tccccagagc | 720 |
| cagaggccag tgggcgaggg gaacgcctgg gcaggaaggt ggcccctttg gccaccaccg | 780 |
| aagactctct ggcttccatc ccctttattg atgagccac cagccccagc attgacctcc | 840 |
| aagccaagca cgtccctgcc tctgctgtgg tctccagtgc catgaactca gccctgtcc | 900 |
| tgggcaccag cccatcttcc ccgaccttca ctttcaccct cggacgcat tactcgagg | 960 |
| actgcagcag catcaaggct ggccgcccgt cctcctacct gctggccatc accacggagc | 1020 |
| gctccaagtc ctgcatgat ggactcaaca ccttcgcga cgagggccgg gttctgcggc | 1080 |
| gcctgccaaa ccgcataccc agcctgcgga tgctccggag cttcttcacc gacgggtcct | 1140 |
| tggatagctg gggcacctct gaagatgctg acgtcccttc taagcgacac tcaacctctg | 1200 |
| acctctcaga tgcgaccttc agcgatatca ggagagaagg ctggttgat tataagcaga | 1260 |
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| cggcgggggc tgcggcggcc ggcgaggct gaggaccggg atgacatgct gggctggatc | 1440 |
| agagcgatcc gggagaacag cagggccgag ggcgaggacc ccggctgtgc caaccaagct | 1500 |
| ctgatcagca agaagcttaa tgattatcgc aaagttagcc atagctctgg gccccaaagct | 1560 |
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| ttaatcgtgg ctgcatgctg tcgcattgtg gaggcacgag ggctggagtc cacaggcatt | 1860 |
| taccgagtgc ccggcaacaa tgcagtgggtg tccagcctac aggagcagct caaccgccc | 1920 |
| cctgggtgaca tcaacctgca ggatgagcgc tggcaagacc tcaatgtgat cagcagcctg | 1980 |
| ctcaagtcct tcttccgaaa gctgcccag cctcttttca ctgatgacaa atacaacgac | 2040 |
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| accatcgctg accactctga gaaaaacaag atggaacccc ggaacctggc cctgggtctt | 2220 |
| gggccgacac tggtaggagc gtctgaggac aacatgacag acatggtgac ccacatgcct | 2280 |
| gaccgctaca agatcgtgga gacactgatc cagcactcag actgggttctt cagtgcgaa | 2340 |

234

gaggacaagg gagagagaac ccctgtgggc gacaaggagc ctcaggcagt gccaacatt 2400
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 <211> 3186
 <212> DNA
 <213> Homo sapien

<400> 222
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| | |
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| acctctcaga tgcgaccttc agcgatatca ggagagaagg ctggttgat tataagcaga | 1260 |
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| ccgcgctgcg ggcgcgctcg ctctcgctga gcaaggagcg gcgggagccc gggccggcg | 1380 |
| cggcgggggc tgcggcgcc ggcgcaggtg aggacgaggc ggcgccgctc tgcacggct | 1440 |
| cctgcctcgt ggacatctcc tacagcgaga ccaagaggag gcacgtgttc cggctgacca | 1500 |
| ccgctgactt ctgtgaatat ctctttcagg ctgaggaccg ggatgacatg ctgggctgga | 1560 |
| tcagagcgat cggggagaac agcagggccg agggcgagga ccccggtgt gccaccaag | 1620 |
| ctctgatcag caagaagctt aatgattatc gcaaagttag ccatagctct gggcccaaag | 1680 |
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| ctgcagcccc caaaaccccc tggggcatca acatcatcaa gaaaaataag aaggccgctc | 1860 |
| cgagggcggt tggggtcagg ctggaggagt gccagccagc cagggagaac cagcgctcc | 1920 |
| ccttaatcgt ggctgcatgc tgcgcattg tggaggcacg agggctggag tccacaggca | 1980 |
| tttaccgagt gcccggcaac aatgcagtgg tgtccagcct acaggagcag ctcaaccgcg | 2040 |
| ggcctggtga catcaacctg caggatgagc gctggcaaga cctcaatgtg atcagcagcc | 2100 |
| tgtcaagtc cttcttcoga aagctgccc agcctctttt cactgatgac aaatacaacg | 2160 |
| acttcacga ggccaaccgc attgaggacg cgcgggagcg aatgaggacg ctgcggaagc | 2220 |
| tgatccggga tctcccagga cactactatg aaacgctcaa attccttggt ggccatctca | 2280 |
| agaccatcgc tgaccactct gagaaaaaca agatggaacc ccggaacctg gccctggtct | 2340 |
| ttgggcccgc actggtgagg acgtctgagg acaacatgac agacatggtg acccacatgc | 2400 |
| ctgaccgcta caagatcgtg gagacactga tccagcactc agactggttc ttcagtgcg | 2460 |
| aagaggacaa gggagagaga acccctgtgg gcgacaagga gcctcaggca gtgccaaca | 2520 |
| ttgagtacct cctgccaac attggcagga cagtgcccc tggcgaccgc gggtcagatt | 2580 |
| ctaccacctg tagttcagcc aagtccaagg tacgtatgaa ggcaattctg aaggcttgat | 2640 |
| ccctgtacaa ggcagcccac tttggttttt gttcaaggga attgaggga tggcagttgg | 2700 |
| accatgggga aagttgatgg tccctgggag ggaaggcagg aggtaccgag tgccaagggt | 2760 |
| aagctgagaa attgcttacc ttggcagtg ttggtgaggc atctgctgta gtagaaggac | 2820 |
| ctggcctggg agttatgtgg ctaggaggca atgtcactca gtagttagaa gcacagactc | 2880 |

236

| | | | | | | |
|-------------|------------|-------------|------------|------------|------------|------|
| tgcaagtcaga | cagtcctggg | tttgagttct | ggctccacca | tttagtagtt | tggaacattg | 2940 |
| ggcaagttac | ttaaccactt | tctgatcctt | agcttcctca | tctataaaat | gggaatatca | 3000 |
| gtaaatctgt | ggggtgctat | aataaataaa | acagatatcc | tttaaggtct | ttggagagcc | 3060 |
| taaagcaagc | agaaggaaat | aaagagagga | gcagaaatcc | atgaaataga | aaacagttga | 3120 |
| aaaaaagcaa | tgaaacaaaa | agctgggttct | ttgaaaaaaa | atcagtgaaa | ttgataaacc | 3180 |
| tctagc | | | | | | 3186 |

<210> 223

<211> 2861

<212> DNA

<213> Homo sapien

<400> 223

| | | | | | | |
|-------------|-------------|------------|-------------|------------|------------|------|
| cagactggag | tgccagcagg | ccttgtcaca | ctggctgtca | aaccaggtag | cccgccgggc | 60 |
| gggggagaga | cggtgcccag | ccatggcccc | ccgggcccgc | agcgctccc | aggaccggtt | 120 |
| ggaggagggtg | gctgcccccc | gcccgtggcc | ctgctccacc | tcccaggatg | ctttgagcca | 180 |
| gctggggccag | gagggctggc | accgagctcg | ctcagatgac | tacttgagcc | ggggccaccg | 240 |
| ttctgccgag | gcactggggc | caggggcact | ggtgtcacc | cgctttgagc | ggtgtggctg | 300 |
| ggcttcccag | cgctcgtctg | cccgccccc | cgctgccc | actcgggacc | tgccagggcc | 360 |
| ccaggcccca | accccgctctg | gcctgcaggg | cctggatgac | ctcgggtaca | tcggctaccg | 420 |
| gagctacagc | ccatcattcc | agcgaccgga | ccggcctcct | ccatgcgctc | tccttccggg | 480 |
| actcaccctt | tggggggctg | cctaccctca | acctggccca | gtcccctgcg | tcattcccac | 540 |
| cagaggcctc | cgagccaccc | agggttgtac | ggccggaacc | cagcaccg | gccctggagc | 600 |
| ctcctgcgga | ggatcgcggc | gatgagggtg | tcctgaggca | gaagccccg | acgggcccga | 660 |
| aggttcagct | gacccccgca | agacagatga | accttggtatt | tggtgacgag | tcccagagc | 720 |
| cagaggccag | tgggcgaggg | gaacgcctgg | gcaggaagg | ggcccctttg | gccaccaccg | 780 |
| aagactctct | ggcttccatc | ccctttattg | atgagccac | cagccccagc | attgacctcc | 840 |
| aagccaagca | cgtccctgcc | tctgctgtgg | tctccagtgc | catgaactca | gcccctgtcc | 900 |
| tgggcaccag | cccatcttcc | cagaccttca | ctttcaccct | cggacgcat | tactcgcagg | 960 |
| actgcagcag | catcaaggct | ggccgcccgt | cctcctacct | gctggccatc | accacggagc | 1020 |
| gctccaagtc | ctgcgatgat | ggactcaaca | ccttccgcga | cgagggccgg | gttctgcggc | 1080 |
| gcctgccaaa | ccgcataccc | agcctgcgga | tgctccggag | cttcttcacc | gacgggtcct | 1140 |
| tggtatagctg | gggcacctct | gaagatgctg | acgctccttc | taagcgacac | tcaacctctg | 1200 |
| acctctcaga | tgcgaccttc | agcgatatca | ggagagaagg | ctgggtgtat | tataagcaga | 1260 |

237

ttctcaccaa gaaggggaag aaagcgggca gcggcctgcg ccagtgggaag cgggtgtacg 1320
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 ctcgagcag gaggcgcaca agcctggggc gggggccaca gcgccgggga ctcaggagcg 2700
 gccgccgggg agccgatgcc cggcgccggc ggccgatgcc ccgcgcgcc gccaccgcg 2760
 cccccggacc cggcagtccc ccggcgcgcg gggaggggccc gccggccgcg gcgacgcgct 2820
 ccattgtgtc gggctaatac aacctgtcac catggaccgg a 2861

<210> 224
 <211> 3118
 <212> DNA
 <213> Homo sapien

<400> 224

238

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|-------------|-------------|-------------|------------|-------------|-------------|------|
| cagactggag | tgccagcagg | ccttgtcaca | ctggctgtca | aaccaggtag | cccgccgggc | 60 |
| gggggagaga | cggtgcccag | ccatggcccc | ccgggcccgc | agcgctccc | aggaccggtt | 120 |
| ggaggagggtg | gctgcccccc | gcccgtggcc | ctgctccacc | tcccaggatg | ctttgagcca | 180 |
| gctgggcccag | gagggctggc | accgagctcg | ctcagatgac | tacttgagcc | gggcccaccg | 240 |
| ttctgccgag | gcaactggggc | caggggcaact | ggtgtcaccc | cgctttgagc | ggtgtggctg | 300 |
| ggcttcccag | cgttcgtctg | cccgcacccc | cgctgccc | actcgggacc | tgccagggcc | 360 |
| ccaggcccca | accccgctctg | gcctgcaggg | cctggatgac | ctcgggtaca | tgggtaccg | 420 |
| gagctacagc | ccatcattcc | agcgaccgga | ccggcctcct | ccatgcgctc | tccttccggg | 480 |
| actcaccctt | tggggggctg | cctaccttca | acctggccc | gtcccctg | tcattcccac | 540 |
| cagaggcctc | cgagccaccc | agggttgtac | ggccggaacc | cagcaccg | gcccctggagc | 600 |
| ctcctgcgga | ggatcgcggc | gatgagggtg | tcctgaggca | gaagccccg | acgggcccga | 660 |
| aggttcagct | gacccccgca | agacagatga | accttggatt | tggtgacgag | tcccagagc | 720 |
| cagaggccag | tgggagggg | gaacgcctgg | gcaggaagg | ggccccttg | gccaccaccg | 780 |
| aagactctct | ggcttccatc | ccctttattg | atgagcccac | cagccccagc | attgacctcc | 840 |
| aagccaagca | cgctccctgcc | tctgctgtgg | tctccagtgc | catgaactca | gcccctgtcc | 900 |
| tgggcaccag | cccatcttcc | ccgaccttca | ctttcacct | cggacgcat | tactcgagg | 960 |
| actgcagcag | catcaaggct | ggccgcccgt | cctcctacct | gctggccatc | accacggagc | 1020 |
| gctccaagtc | ctcgatgat | ggactcaaca | ccttcgcgga | cgaggggccg | gttctgcggc | 1080 |
| gcctgccaaa | ccgcataccc | agcctgcgga | tgctccggag | cttcttcacc | gacgggtcct | 1140 |
| tggatagctg | gggcacctct | gaagatgctg | acgtccttc | taagcgacac | tcaacctctg | 1200 |
| acctctcaga | tgcgaccttc | agcgatatca | ggagagaagg | ctggttgtat | tataagcaga | 1260 |
| ttctcaccaa | gaaggggaag | aaagcgggca | gcggcctg | ccagtgggaag | cggtgtacg | 1320 |
| ccgcgctg | ggcgcgctg | ctctcgctga | gcaaggagcg | gcgggagccc | gggcccggcg | 1380 |
| cggcgggggc | tgcgggggcc | ggcgaggtg | aggacgaggc | ggcgcccgtc | tgcatcggtc | 1440 |
| cctgcctcgt | ggacatctcc | tacagcgaga | ccaagaggag | gcacgtgttc | cggtgacca | 1500 |
| ccgctgactt | ctgtgaatat | ctctttcagg | ctgaggaccg | ggatgacatg | ctgggctgga | 1560 |
| tcagagcgat | ccgggagaa | agcagggccg | agggcgagga | ccccggctgt | gccaaccaag | 1620 |
| ctctgatcag | caagaagctt | aatgattatc | gcaaagtgag | ccatagctct | ggcccaaaag | 1680 |
| ctgattcctc | ccccaaaggc | tctcgcgcc | tggggggcct | caagtctgag | ttcctcaagc | 1740 |
| agagtgcggc | acgtggcctc | aggactcagg | acctgcccgc | agggagcaag | gatgacagtg | 1800 |
| ctgcagcccc | caaaaacccc | tggggcatca | acatcatcaa | gaaaaataag | aaggccgctc | 1860 |

cgagggcggtt tggggtcagg ctggaggagt gccagccagc cacggagaac cagcgcggtcc 1920
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 aagtccaagg gttcgtgggc cccaagaag gagccgtacg cccgggagat gctggcgatc 2820
 tccttcactc cggccgtcaa ccgcaagcgc aagaagcggc gggaggcgcg ggggctgggc 2880
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 ccggggactc aggagcggcc gccggggagc cgatgcccgg cgccggcggc cgatgccccg 3000
 cgccgccgcc accgcgccc ccggacccgg cagtcccccg gcggcgcggg aggggcccgc 3060
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<210> 225

<211> 1018

<212> DNA

<213> Homo sapien

<400> 225

gaagcgacg atggcgcgct caatgcggtt ggctctttt cactgatggg gcccttctct 60
 tctgacctgc tgaaccttgg tgtccatgtc ctggagacgg gggcagggac cccttttctg 120
 ggatcagcat gcagctcaga tggatttggc tcccaaatac acacagctgg gctaccccag 180
 gtcaggtgca caccgagtg tagctgtgac aaatacaacg acttcacga ggccaaccgc 240
 attgaggacg cgcgggagcg aatgaggacg ctgcggaagc tgatccggga tctcccagga 300
 cactactatg aaacgctcaa attccttgtg ggccatctca agaccatcgc tgaccactct 360

240

gagaaaaaca agatggaacc ccggaacctg gccctggtct ttgggcccac actggtgagg 420
 acgtctgagg acaacatgac agacatggtg acccacatgc ctgaccgcta caagatcgtg 480
 gagacactga tccagcactc agactggttc ttcagtgacg aagaggacaa gggagagaga 540
 acccctgtgg gcgacaagga gcctcaggca gtgcccaca ttgagtacct cctgcccac 600
 attggcagga cagtgtcccc tggcgacctg gggctcagatt ctaccacctg tagttcagcc 660
 aagtccaagg gtctgtgggc cccaagaag gagccgtacg cccgggagat gctggcgatc 720
 tccttcactc cggccgtcaa ccgcaagcg aagaagcggc gggaggcgcg ggggctgggc 780
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 cgccgccgcc accgcggccc ccggacctcg cagtcccccg gcggcgcggg aggggcgcc 960
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<210> 226

<211> 1844

<212> DNA

<213> Homo sapien

<400> 226

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 tcaccactgc tagtcatcca ggtgggggac cgacactctc tggagaccag cgatgccacg 180
 cccagaagct tctctttatc tctaactcct gcctcagtca cccaatggg ccgcctcttc 240
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 aggacagatg atttcatgc tcagagacag atgagggcca ctccctttgt ggctgcagcc 360
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 ctgacagagg cacacaggag ctccctagtc accagaggca ggctcaggag gggccagaag 480
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 gcgccctgtg tgtcgtgtgt ggtcgcccat cttgcttttc tcaccttggt cagggggagg 600
 ggtccggaga ggggggcgtc taacttgcct gccagagagt gtggattaac cgcacctgcc 660
 cactacctg tgggacccca ggaggccctt ggaccaacct gctccctctt tagccttgga 720
 ggggacccac caggacgtgt ttctggttcc ttctccacc cagtgatatt aaggagtg 780
 gacccaagtc ccatagaaat catgctttta gtctccttca taactgggtg ataactgggg 840
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 caccagccca ctccacctcc tgcgtccac ccacttcatt tttgccctt tatccattat 960

241

tcatgtggtc cctcttctct gttgtgtgct cgggggtgga tgtagggcac ccacctctct 1020
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 gctccattgt gtcgggctaa tccaacctgt caccatggac cgga 1844

<210> 227

<211> 1003

<212> DNA

<213> Homo sapien

<400> 227

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 cctagatttg ggccagcggg ggtagtctac tgagacgaga gggcggacac ggggactgga 180
 agagaggagc gtttatatga tgcgccctg ggtgactgga ottggactgg ggcttgatga 240
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 cccaagaagg agccgtacgc ccgggagatg ctggcgatct ccttcatctc ggccgtcaac 420
 cgcaagcgca agaagcggcg ggaggcggg gggctgggca gcagcaccga cgacgactcg 480
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 cwggggccgc tgccctggcg cgtcgcccc gagggcccc gacgcctcag tccccggcg 600
 gcgcggagg agcggccggc cgcggacacg cgctccattg tgcgggcta ctccacctg 660
 tccaccatgg accgcagcgt gtgctcgggc gctagcggtc ggcgggagg ggcgggggac 720

242

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gaggcggacg acgagcgtag cgagctgake cacgtggaga cggacactga gggcgcggcg 780
ggcgcggggc ctggggggcg cctgacacgc cggccgtcct tcagctcgca ccacctcatg 840
ccctgcgaca ctctggcgcg ccgccgcctg gcccggggccc gccagacgg cgagggcgcg 900
ggcggggcg gtccccgcgc cccggagccg cccggctcgg cgtcgtccag cagccaggag 960
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```

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<210> 228
<211> 989
<212> DNA
<213> Homo sapien

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<220>
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<222> (141)..(141)
<223> n=a,c,g or t

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<220>
<221> misc_feature
<222> (147)..(147)
<223> n=a,c,g or t

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<220>
<221> misc_feature
<222> (206)..(206)
<223> n=a,c,g or t

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<400> 228
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agaacccttg tgggtgacaa ggagcntcag gcagtgccca acattgagta cctcttgccc 240
aacattggca ggacagtgcc ccctggygac cggggtcagy ggacctgttg gagatttaaa 300
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gccggccgcg gacacgcgct ccattgtgtc gggctactcc accctgtcca ccatggaccg 660
cagcgtgtgc tcgggcgcta gcggtcggcg ggcaggggag ggggacgagg cggacgacga 720
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243

ggggcgccctg acacgccggc cgtcccttcag ctgcaccac ctcatgccct gcgacactct 840
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 ccgcgccccg gagccgcccc gctcggcgtc gtccagcagc caggagtcgc tgcggccccc 960
 ggcgggcgcg ctggcctccc ggccctcgc 989

<210> 229
 <211> 776
 <212> DNA
 <213> Homo sapien

<400> 229
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 aaaccaccaa tgtgggaggg ggtgctaaaa ctttaaaaaa aatctctact gtgcaaatat 180
 cattattcac tgcagacttc cataagagta aataaaaatg aatatgcagt ggcgacattg 240
 ttttataagt cactggtact atggacaact ccatagtga tggagatact tgcagagctt 300
 gtcattgcaca ctaagagttt aaaatgtgag ctcatatta atcatagttt caaaattatc 360
 aaataaaacc agtgaagatc tgaagatgca aacatttcaa ctatgaagat ttacatttca 420
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 tttaatgcct ttacaatacc ttttaatttat taggatctca gaatcattgt ttactatccc 540
 ttatttgaca aaaagtcaa tgtgtatggt ctacctcaa cggaaatggt tacaagggtca 600
 agacttaatt caattcagac aagaccaaag ttgcttgact tcaattcctg tgcattagtg 660
 tgatgatttc tgtcacatag cagcattccg attctatgta actgaatgga gatgataagt 720
 gctttcccct ctttatttaa aaaagattaa aaggaatcaa agaaataatg tatggc 776

<210> 230
 <211> 831
 <212> DNA
 <213> Homo sapien

<400> 230
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 gtccctcttta ccacctatca aactgtgtt catgggaaca gcagctggag gcacttaaac 180
 caccaatgtg ggaggggggtg ctaaaacttt aaaaaaatc tctactgtgc aaatatcatt 240
 attcactcag acttcataa gagtaaataa aaatgaatat gcagtggctg acattgtttt 300
 aaagtcactg gtactatgga caactccata gtgaatggag atacttgag agcttgtcat 360

244

gcacactaag agttttaaag gtgagctcat tattaatcat agtttcaaaa ttatcaaata 420
 aaaccagtga agatctgaag atgcaaacat ttcaactatg aagatttaca tttcactttc 480
 taattttatta aacatctgtg tgccttttta totttggttt ctttttaaaaa gtatatttaa 540
 tgcctttaca atacctttaa tttatttagga totcagaatc attgtttact atcccttatt 600
 tgacaaaaag tcaaatgtgt atgttctacc tccaacggaa atgtttacaa ggtcaagact 660
 taattcaatt cagacaagac caaagttgct tgacttcaat tcctgtgcat tagtgtgatg 720
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 cccctcttta tttaaaaaag attaaaagga ataaaagaaa taatgtatgg a 831

<210> 231
 <211> 333
 <212> DNA
 <213> Homo sapien

<400> 231
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 gagaatttgg ttttattcat gttaagtttt aagatgcttg tcagaagttg aagaggaagt 180
 gtcaagtatg tatttgcata taaaatctgg agctcaggca gaaatgattc aagtattatt 240
 actgggcaga tccaaacgtt tagaagtcag gaagaagaga acccagtaaa gatactaagg 300
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<210> 232
 <211> 435
 <212> DNA
 <213> Homo sapien

<400> 232
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 gtaaagccag ccagactgtt ggtatgtata atgaaggaaa gaggagtcaa ggatgatgcc 180
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 tataaaatct ggagctcagg cagaaatgat tcaagtatta ttactgggca gatccaaacg 360
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 gtaaggccgg gtgca 435

<210> 233
 <211> 492

245

<212> DNA

<213> Homo sapien

<400> 233

| | |
|--|-----|
| gatgaatcct acatcagtga actgggcatg ggctcagcaa tgcccaattg accgtgtgtg | 60 |
| tccttgtatg gagatggctg gccccgaagc tccccagagg gattgggtgct agaacatgga | 120 |
| tggggacttt gaaagagggg gcgggtgacg gaggaaacgt gtagggccat tcgtgccttc | 180 |
| cgggtgcatt cctcatggcc agtcgcagac atgtctctaa ccttactcca ggctcctgct | 240 |
| tctcaggcgt ggtgtccatc acatgccgcc ctgcgaatgt tgagggtgtg ggctctcgtg | 300 |
| tgggagttag aagacctggg tttttgtcca gctttgccat tcatcacctc catgactctg | 360 |
| ggcacatcag ggtccttcgt ggtctcagtt tcctctttgt gtaaaatggg aattatgggt | 420 |
| gtttaacctt ctacgcagat ggcaggaaag ggacacagcc ggcgcgatgat tgtgggaggc | 480 |
| tcagggatgg ag | 492 |

<210> 234

<211> 1808

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1690)..(1690)

<223> n=a,c,g or t

<400> 234

| | |
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| tccttgtatg gagatggctg gccccgaagc tccccagagg gattgggtgct agaacatgga | 120 |
| tggggacttt gaaagagggg gcgggtgacg gaggaaacgt gtagggccat tcgtgccttc | 180 |
| cgggtgcatt cctcatggcc agtcgcagac atgtctctaa ccttactcca ggctcctgct | 240 |
| tctcaggcgt ggtgtccatc acatgccgcc ctgcgaatgt tgagggtgtg ggctctcgtg | 300 |
| tgggagttag aagacctggg tttttgtcca gctttgccat tcatcacctc catgactctg | 360 |
| ggcacatcag ggtccttcgt ggtctcagtt tcctctttgt gtaaaatggg aattatgggt | 420 |
| gtttaacctt ctacgcagat ggcaggaaag ggacacagcc ggcgcgatgat ctgggaggcc | 480 |
| tccagggatg gagagtggcc tggctggcaa cggcacagga gctgggctgg tgatgaaggt | 540 |
| caagcaggag aagccggagc ggctgctgca gacgctggcg ccgcaggcca tgcttgtgga | 600 |
| gaaggacaag gagaacatct ttcagcagca ccggggcctc ccgccacgcc agaccatggg | 660 |
| gctggcctcg agccctgggg ggacaggagg agtctgggag tccaagggtg gccctccca | 720 |
| ctgagcagtg atgcggggct ggcagtgcct gggctcccgg gtcagcctcc ggccccctgg | 780 |

246

| | | | | | | |
|-------------|------------|-------------|-------------|------------|-------------|------|
| agccccctcgc | tttcctccgg | cgaggggtcac | tttgtatgcc | tggactgcgg | gaagagggttc | 840 |
| agctggtggt | cgtccctgaa | gatccaccag | cgcaccacaca | ccggggagaa | gccgtacctc | 900 |
| tgcggcaagt | gcggcaagag | cttcagccag | aagccgaacc | tggcgcgcca | ccagcggcac | 960 |
| cacacgggcg | agcgaccctt | ctgctgcccc | gagtgcgcgc | ggcgcttcag | ccagaagcag | 1020 |
| cacctgctca | agcaccagaa | gaccactcc | cggccccgcca | cccactcgtg | ccccgagtgc | 1080 |
| gagcgctgct | tccgtcacca | ggtgggcctc | cgcattccacc | agcgcgcgca | cgcgccgggac | 1140 |
| cgccagggct | cccgcgccgg | cctgcacgag | ctgattcagg | acgcggcggc | gcgcgccggcc | 1200 |
| tgtcgctgct | agccggggcc | gccgcggggg | cgcgccgagt | gggcctggct | ggggctctgc | 1260 |
| cagggctggt | ggggccagcc | cggggccccg | gccgcggtct | ccggccccga | ggggccgggc | 1320 |
| gagccgcgcc | agttcatctg | caacgagtgt | ggcaagagct | tcaactggtg | gtcgtcgctg | 1380 |
| aacatccacc | agcgcattca | caactggcag | cgcacctatg | cgtgccccga | gtgcggccgc | 1440 |
| cgcgttcagc | cagaagccca | acttgacgcg | gcacctgcgc | aaccacacag | gcgaagcgcc | 1500 |
| cggacccttg | cccgcactgt | ggccgcggct | tcagccagaa | gcagcacctg | ctcaagcacc | 1560 |
| agcgcgtgca | ccgcgcggcc | cctgcgtgca | gccccaaagg | ggaggcgcgc | tagtggactg | 1620 |
| gacctcagcg | gacctgtggt | ggtgcggggg | atgtttgcgg | ggtgtgtgtg | gggatgtggg | 1680 |
| ggtggccagn | attgctggct | cctagaacct | attagagcgg | aaccggtgta | ttccttaatg | 1740 |
| ctctgaatgg | ctgagaacag | ttctagaacc | gtcccatagg | gtgctggtaa | aggtcccagc | 1800 |
| gtgggttg | | | | | | 1808 |

<210> 235

<211> 1271

<212> DNA

<213> Homo sapien

<400> 235

| | | | | | | |
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| acctgagcac | acaggtagag | gcgggtcccc | aaagacttgg | cctccccctca | ttcctgtcct | 120 |
| ctgtgtttcc | ccctttgaat | ttctcacttc | ttcctcttgg | gtcctcttcc | ttctgtctcc | 180 |
| atttctgttc | ttacgtaagc | cacaggctgc | ttccccctga | gccctggtat | ggcccagagc | 240 |
| agaggcaccg | aggcttgagg | gaggagctgc | tctgggaggt | cccggacagt | ggaaggcctg | 300 |
| ctactacctg | gagtggctgt | taggtcctaa | tacctcttgg | gaggcagggt | gggtgaagta | 360 |
| ggactgtctt | tgatttgcct | tgggggtctc | gctctgtgga | gaccagggcc | catccttctg | 420 |
| tctcctgaa | tttgtggcct | gggctctgcc | ctcctcggtc | tgagttcccc | ttaccaaggt | 480 |
| ggcttctctg | tccactagcc | cctctgcgcc | tcttcagggt | gatgttaagt | ccagttgggt | 540 |

247

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agaggtttcc caagatgtgg catgcagaag ctcacagagt ggccccaagg gaggaggggtg      600
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gaggactgga cattaccatt tgtcacacgc aggcaggtcg tcctaaattc acctcataat     1200
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```

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<210> 236
<211> 2520
<212> DNA
<213> Homo sapien

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<400> 236
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agaggcttgt acagatactg cccgatgcat ccggctcagg cttgccgccc tgtgggtgctc     180
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tggtcgtccc tgaagatcca ccagcgcacc cacaccgggg agaagccgta cctctgcggc     780
aagtgcggca agagcttcag ccagaagccg aacctggcgc gccaccagcg gcaccacag     840

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248

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<210> 237

<211> 2489

<212> DNA

<213> Homo sapien

<400> 237

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| ccaactggct ggaaggagt atggcttagg aggagtgagt ggcagcgggg acgctggcag | 120 |
| agaggcttgt acagatactg cccgatgcat ccggctcagg cttgccgccc tgtggtgctc | 180 |
| ctcccaaact cagggagcag ccagctgcag ctctgtctga cttatccac ccagcgcag | 240 |
| gtcatccaac ggtgacttat ggccccggcc tcctggctcg atgaggatgg caggaaaggg | 300 |
| acacagccgg cgctgatgct gggaggcctc cagggatgga gagtggcctg gctggcaacg | 360 |
| gcacaggagc tgggctggtg atgaaggta agcaggagaa gccggagcgg ctgctgcaga | 420 |
| cgctggcgcc gcaggccatg cttgtggaga aggacaagga gaacatcttt cagcagcacc | 480 |
| ggggcctccc gccacgccag accatggggc ggcctcgagc cctgggggga caggaggagt | 540 |
| ctgggagtcc aaggtgggcc cctccactg agcaggatgc ggggctggca ggccgggctc | 600 |
| ccgggtcagc ctccggcccc ctgagccctc cgctttcctc cggcgagggt cactttgtat | 660 |
| gcctggactg cgggaagagg ttcagctggt ggtcgctcct gaagatccac cagcgcaccc | 720 |
| acaccgggga gaagccgtac ctctgcggca agtgcggcaa gagcttcagc cagaagccga | 780 |
| acctggcgcg ccaccagcgg caccacacgg gcgagcgacc cttctgctgc ccgagtgcg | 840 |
| cgcggcgctt cagccagaag cagcacctgc tcaagcacca gaagaccac tcccggcccg | 900 |
| ccaccactc gtgccccgag tgcgagcgt gcttcctca ccaggtaggc ctccgcatcc | 960 |
| accagcgcg cgcacgcccgg gaccgcccag gctcccgcgc cggcctgcac gagctgattc | 1020 |
| aggacgcggc ggcgcgcgg gcctgtcgcc tgcagccggg gccgcgcgg gggcgccccg | 1080 |
| agtgggcctg gctggggctc tgccagggt ggtggggcca gccgggggccc cgggcgcgg | 1140 |
| tctccggccc cgagggggcg ggcgagccgc gccagttcat ctgcaacgag tgtggcaaga | 1200 |
| gcttcacctg gtggtcgctg ctgaacatcc accagcgcat ccacactggc gagcgccccct | 1260 |
| atgctgccc cgagtgcggc cgcgcttca gccagaagcc caacttgacg cggcacctgc | 1320 |
| gcaaccacac aggcgagcgc ccgcaccct gccgcactg tggccgcggc ttccgccaga | 1380 |
| agcagcacct gctcaagcac ctgpcgacgc acctgcccgg cggccaggct ggcacctgcc | 1440 |
| ccagctgcgg taagagctgc cgcagcccg ccgcgctgc cggccaccag cgcgcccacg | 1500 |
| ctgtcgctga gcccgccgtt ccggccgggg aaccggggca ccagccgcag gccgaggcca | 1560 |
| tcccgggctt ggccgcgagg ccgcggagct cccaacggtc cccggggggc cgggacacac | 1620 |
| tgtggggccg gggacaagcg ggcctcgctg ggcctggcga gccgcgccag ttcactctga | 1680 |
| acgagtgcgg caagagcttc tcgtggtggt cggcgctcac catccaccag cgcattccaca | 1740 |
| cgggtgagcg gccctaccg tgccccgagt gcggccgccc cttcagccag aagcccaacc | 1800 |

250

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 <211> 2457
 <212> DNA
 <213> Homo sapien

<400> 238
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<211> 2120

<212> DNA

<213> Homo sapien

<400> 239

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| tagccacaaa | gtcaaagatg | gcaggaaaagg | gacacagccg | gcgctgatgc | tgggaggcct | 120 |
| ccagggatgg | agagtggcct | ggctggcaac | ggcacaggag | ctgggctggt | gatgaaggtc | 180 |
| aagcaggaga | agccggagcg | gctgctgcag | acgctggcgc | cgcaggccat | gcttgtggag | 240 |
| aaggacaagg | agaacatctt | tcagcagcac | cggggcctcc | cgccacgcca | gaccatgggg | 300 |
| cggcctcgag | ccctgggggg | acaggaggag | tctgggagtc | caaggtgggc | ccctcccact | 360 |
| gagcaggatg | cggggctggc | aggccgggct | cccgggtcag | cctccggccc | cctgagcccc | 420 |
| tcgctttcct | ccggcgaggg | tacttttgta | tgcttgact | gcgggaagag | gttcagctgg | 480 |
| tggtcgtccc | tgaagatcca | ccagcgcacc | cacaccgggg | agaagccgta | cctctgcggc | 540 |
| aagtgcggca | agagcttcag | ccagaagccg | aacctggcgc | gccaccagcg | gcaccacacg | 600 |
| ggcgagcgac | ccttctgctg | ccccgagtgc | gcgcggcgct | tcagccagaa | gcagcacctg | 660 |
| ctcaagcacc | agaagacca | ctcccggccc | gccaccact | cgtgccccga | gtgcgagcgc | 720 |
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| tcggcgctca | ccatccacca | gcgcatccac | acgggtgagc | ggccctacc | gtgccccgag | 1560 |
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| aagcaccagc | gcgtgcaccg | cgcggccctt | gcgtgcagcc | ccaaggagga | ggcgcgctag | 1740 |
| tggactggac | ctcagcggac | ccgtggtggt | gcgggggatg | tttgcggggt | gtgtgtgggg | 1800 |
| agtgggggtg | gccaggattg | ctggctctta | gaaccctta | gagcgggacc | ggtggattcc | 1860 |

253

ttaaggctct gaagggtga gaacagttct agaagcgcca cccactcgtg ccccgagtgc 1920
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<211> 757
<212> DNA
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<400> 241
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254

| | |
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| gttttacctt ctcagcagat ggcaggaaag ggacacagcc ggcgctgatg ctgggaggcc | 480 |
| tccagggatg gagagtggcc tggctggcaa cggcacagga gctgggctgg tgatgaagggt | 540 |
| caagcaggag aagccggagc ggctgctgca gacgctggcg ccgcaggcca tgcttgtgga | 600 |
| gaaggacaag gagaatgttt tgtggaccac tttggttttc ttttttgcgt gtggcagttt | 660 |
| taagttatta gtttttaaaa tcagtacttt ttaatggaaa caacttgacc aaaaatttgt | 720 |
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<210> 242

<211> 2280

<212> DNA

<213> Homo sapien

<400> 242

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| ccagggatgg agagtggcct ggctggcaac ggcacaggag ctgggctggg gatgaaggtc | 180 |
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| cggcctcgag ccctgggggg acaggaggag tctgggagtc caaggtgggc ccctcccact | 360 |
| gagcaggatg cggggctggc aggccgggct cccgggtcag cctccggccc cctgagcccc | 420 |
| tcgctttcct ccggcgaggg tcactttgta tgcctggact gcgggaagag gttcagctgg | 480 |
| tggtcgtccc tgaagatcca ccagcgcacc cacaccgggg agaagccgta cctctgcggc | 540 |
| aagtgcggca agagcttcag ccagaagccg aacctggcgc gccaccagcg gcaccacacg | 600 |
| ggcgagcgac ccttctgctg ccccgagtgc gcgcggcgct tcagccagaa gcagcacctg | 660 |
| ctcaagcacc agaagaccca ctcccggccc gccacccact cgtgccccga gtgcgagcgc | 720 |
| tgcttccgtc accaggtggg cctccgcac caccagcgcg cgcacgcccg ggaccgccag | 780 |
| ggctcccgcg ccggcctgca cgagctgatt caggacgcgg cggcgcgccg ggcctgtcgc | 840 |
| ctgcagccgg ggccgcccgc ggggcgcccc gagtgggcct ggctggggct ctgccagggc | 900 |
| tggtggggcc agcccggggc ccgggcccgc gtctccggcc ccgaggggccc gggcgagccg | 960 |
| cgccagttca tctgcaacga gtgtggcaag agcttcacct ggtggtcgtc gctgaacatc | 1020 |
| caccagcgca tccacactgg cgagcgcccc tatgcgtgcc ccgagtgcgg ccgccgcttc | 1080 |
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255

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| cacctgccccg | gcgcccaggc | tgcgccctgc | cccagctgcg | gtaagagctg | ccgcagccgc | 1260 |
| gccgcgctgc | gcgcccacca | gcgcgcccac | gctgtcgctg | agcccgccgt | tccggccggg | 1320 |
| gaaccggggcg | accagccgca | ggccgaggcc | atccccgggt | tggccgcgag | gccgcggagc | 1380 |
| tcccaacgggt | ccccgggggc | ccgggacaca | ctgtggggcc | ggggacaagc | gggcctcgct | 1440 |
| gggcctggcg | agccgcgcca | gttcatctgc | aacgagtgcg | gcaagagctt | ctcgtggtgg | 1500 |
| tggcgctca | ccatccacca | gcgcatccac | acgggtgagc | ggccctacc | gtgccccgag | 1560 |
| tgcggccgcc | gcttcagcca | gaagcccaac | ctgacgcggc | accggcgcaa | ccacacaggc | 1620 |
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| agtgggggtg | gccaggattg | ctggctotta | gaaccctta | gagcgggacc | ggtggattcc | 1860 |
| ttaaggctct | gaagggctga | gaacagttct | agaagcgtcc | caaaggggtc | tgggaaagggt | 1920 |
| cccagcgtgg | gttgaggag | gagggagat | ccgagttcct | caccgcgggc | cgggatgtga | 1980 |
| ccacctctt | cagaggttgg | acccaggct | tcaagcaccg | agtgagggtg | ctgttgggga | 2040 |
| cgctgggaga | gtctctggtg | tgaagtggct | taggtctgga | ctggtcagct | gtggcaccag | 2100 |
| ccggtcctgc | ccacgcttca | ggatggccgg | gggctgcccc | tgtgggagag | ttgccaaagc | 2160 |
| tccgcgatac | caaggatgga | agccagaggc | tgtggcgagg | gagagccaag | catattccca | 2220 |
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<211> 2641

<212> DNA

<213> Homo sapien

<400> 243

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| gttcttgtat | ggagatggct | ggccccgaag | ctcccagag | ggatttgtgc | tagaacatgg | 120 |
| atggggactt | tgaagagggg | ggcgggtgac | ggaggaaacg | tgtagggcca | ttctgccttc | 180 |
| cgggtgcatt | cctcatggcc | agtcgcagac | atgtctctaa | ccttactcca | ggctcctgct | 240 |
| tctcaggcgt | ggtgtccatc | acatgccgcc | ctgcgaatgt | tgagggtgtg | ggctctcgctg | 300 |
| tgggagttag | aagacctggg | tttttgtcca | gctctgccat | tcatcacctc | catgactctg | 360 |
| ggcacatcag | gggtccttcg | tggctctcagt | ttcctctttt | gtaaaatggg | aattatggct | 420 |
| gttttacctt | ctcagcagat | ggcaggaaag | ggacacagcc | ggcgctgatg | ctgggaggcc | 480 |

256

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| gaaggacaag gagaacatct ttcagcagca ccggggcctc ccgccacgcc agaccatggg | 660 |
| gcggcctcga gccctggggg gacaggagga gtctgggagt ccaaggtagg cccctccac | 720 |
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| caagtgcggc aagagcttca gccagaagcc gaacctggcg cgccaccagc ggcaccacac | 960 |
| gggcgagcga ccccttctgt gccccgagtg cgcgcggcgc ttcagccaga agcagcacct | 1020 |
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| ccaccagcgc atccacactg gcgagcgccc ctatgcgtgc cccgagtgcg gccgcgctt | 1440 |
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| gtcggcgctc accatccacc agcgcattca cacgggtgag cggccctacc cgtgccccga | 1920 |
| gtgcggccgc cgcttcagcc agaagcccaa cctgacgcgg caccggcgca accacacagg | 1980 |
| cgagcggccc tacctgtgtc ccgcctgcgg ccgcggcttc agccagaagc agcacctgct | 2040 |
| caagcaccag cgcgtgcacc gcgcggcccc tgcgtgcagc cccaaggagg aggcgcgcta | 2100 |
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257

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| tcccagcgtg ggttgagggg ggaggggaaga tccgagttcc tcaccgcggg ccgggatgtg | 2340 |
| accaccctct tcagaggttg gaccccaggc ttcaagcacc gagtgagggg tctgttgggg | 2400 |
| acgctgggag agtctctggt gtgaagtggc ttaggtctgg actggtcagc tgtggcacca | 2460 |
| gccggtcctg cccaagcttc aggatggccg ggggctgccc ctgtgggaga gttgccaaga | 2520 |
| ctcggcgata ccaaggatgg aagccagagg ctgtggcgag ggagagccaa gcatattccc | 2580 |
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 <211> 2321
 <212> DNA
 <213> Homo sapien

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258

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<211> 1263

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<213> Homo sapien

<400> 245

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 gagcaggatg cggggctggc aggccgggct cccgggtcag cctccggccc cctgagcccc 420
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259

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aaa 1263

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<210> 246
<211> 336
<212> DNA
<213> Homo sapien

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<400> 246
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ataggaagta ctcttctct tctgtcact gtcacacatg ctccctgagc agaatctagc 180
agctcatctt ctgctatctg caaatgggtca ttgcttctag gttactctaa tgaagcagaa 240
aattccactt caggaagttt tctcaccatg agactaaaat gtactgtgtt gctattgtta 300
ctattagctc tgtttacctg aagagatagt ggaagc 336

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<210> 247
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<212> DNA
<213> Homo sapien

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ataggaagta ctcttctct tctgtcact gtcacacatg ctccctgagc agaatctagc 180
agctcatctt ctgctatctg caaatgggtca ttgcttctag gttactctaa tgaagcagaa 240

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260

aattccactt caggaagttt tctcaccatg agactaaaat gtactgtgtt gctattgtta 300
 ctattagtgc tgtttacctg aagagatagt ggaagc 336

<210> 248
 <211> 528
 <212> DNA
 <213> Homo sapien

<400> 248
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 tcttttaggaa ccatatttct atttctacaa atctcatagc cttgttgat tgtatgcact 180
 gtaggcaatg ggaaaataag tattcaatga atgtcagtga gaaaagaaag aaacgagggc 240
 tatttgtgta ttactcattc aaatggaagg accagggaca tggaatgaat tatattttcc 300
 atattttatg tatttcttat ttatttttat aataaattat gaatggttta aggctgctaa 360
 atattcttct taggttcctt tggaaaaggc aagagttcct gaagttgtag cacatttcaa 420
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 aaactctatt tatgtattct cttttttcat gtcttaagag tgagactc 528

<210> 249
 <211> 528
 <212> DNA
 <213> Homo sapien

<400> 249
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 tggtagcaaa aggttttcta gaattttctg gatgttaaca tgcttaatac aagttctttg 120
 tcttttaggaa ccatatttct atttctacaa atctcatagc cttgttgat tgtatgcact 180
 gtaggcaatg ggaaaataag tattcaatga atgtcagtga gaaaagaaag aaacgagggc 240
 tatttgtgta ttactcattc aaatggaagg accagggaca tggaatgaat tatattttcc 300
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<210> 250
 <211> 1005
 <212> DNA
 <213> Homo sapien

261

<220>
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 <222> (354)..(436)
 <223> n=a,c,g or t

<400> 250
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 tctctggcct tgggtactggc tgcctctga ggcaccttg tgtcttttcc acaatgggtt 960
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<210> 251
 <211> 605
 <212> DNA
 <213> Homo sapien

<400> 251
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 tgttgtggct tttttctgtc tgctgcctaa caaagccccc aggcttagta gctttaaaga 360
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262

tttcacctgg gcttactcat ctgccgagtt cacctgggtg gtggttgagc tggaagttct 480
gatgtgactt ccttcacatg totctggcct tggtaactggc tgtcctctga ggcaccttgg 540
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gtttc 605

<210> 252
<211> 2671
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (84)..(84)
<223> n=a,c,g or t

<220>
<221> misc_feature
<222> (2409)..(2409)
<223> n=a,c,g or t

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atatagatag catgtatatg taggctcatt tgtgggagat tgcaacttta tgtgccccca 180
gttctccttg gttttgtagg aaagctaaaa gaaaaccttg tactctcact aataatgaaa 240
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atgcctggaa taaaatatgg aattcttctg tacctacctc ccccttacag acttttctcc 360
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263

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caagtgccat tataaagttt taaaaattat c 2671

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<210> 253
<211> 2712
<212> DNA

264

<213> Homo sapien

<220>

<221> misc_feature

<222> (84)..(84)

<223> n=a,c,g or t

<400> 253

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gttctccttg gttttgtagg aaagctaaaa gaaaaccttg tactctcact aataatgaaa      240
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ctattcttca gagaatatat gatcagcctg tgtttactat gcacctactc ttataccaga     1500
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265

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aatgagagac aatgcaatat tgtataatto ctggatgatg caattgtttt aattgaattt 2640
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<210> 254

<211> 2736

<212> DNA

<213> Homo sapien

<400> 254

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aattcatagc caatttagaa agggaaaata acctgaaaac caaaatacct cattcatctg 300
aagatgcctg gaataaaata tggaattctt ctgtacctac ctccccctta cagacttttc 360
tcctattttg agagagaaat tcaagaagaa gaatacagct tgttctcttt ccacaaatga 420

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266

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| cacaggcctt cttggagaat gaagaatatc agccccattc aggggttacc aatgtctctc | 540 |
| tgaggtgaca atacattctg gttttccagg acagtcttgg cttaggtctg ctgtccttct | 600 |
| ataaatatta acaatgatcc ctcttatttc caaacgtgtc ccagtttaga caacaaatta | 660 |
| tacagtgtct gcccccaaca cacacacaca cccccacca tctttatggg ttgttgttgt | 720 |
| tttcttgttg tttttaattt tgtagaattg gctttgtctt ctccaaagca gataacagct | 780 |
| taaactaaag agcctagcta cttctttctg actgagcagg gtcatagtaa acagagaaga | 840 |
| atggatcact tcctcctctg aaatctccat caatccactt tctgtccaac tatctctcta | 900 |
| cccagcctat ttttggctct agttttctc tcataacccc tgggctgtga gtccctgagtt | 960 |
| ctgccttcat atggcagagc aagctagtca ttattatgcc aggttaggtg gtggggcaag | 1020 |
| acaaaagata gctcttgggg acacttgctt ggtctgtaga gatccacagg gcactagtag | 1080 |
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| agacaggctt tacgttaacc ttcaccttaa aaaggatatt gccttttttc cttctgttc | 1200 |
| acaaatttgc tccaacacta attcccttgc atttgatttc atcattatga ttgttcatca | 1260 |
| accattcttc acgaaaaatc ctccatcat gtcataataa ggttttatta tttttaatgg | 1320 |
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| cagaaactgt gaatacaaat acatatattt cctacttctc tctttaattg gggcacacag | 1560 |
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| atgcaaaaat agaaggagaa aaaggttagt tagaggcca gaaggagaat taaaacatgg | 1860 |
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| tacttgaaaa cattttggcc attaaactatt tctgttttct aaatacattt gtgtttataa | 1980 |
| aattttaaaa tctatatcac aagccttaga catgcctttc tttgcaataa agtatatata | 2040 |
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| tcttctatgt ttctgactgc aatacagccc gatattgtta ttccctatat cttaatgaaa | 2280 |

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 <211> 579
 <212> DNA
 <213> Homo sapien

<400> 255
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 atatggacta ccaatatgta tgtatacagc atacagcata taaagttaga gggaataata 240
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268

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<211> 241
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a 241

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<212> DNA
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269

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<211> 1406

<212> DNA

<213> Homo sapien

<400> 260

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270

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 <212> DNA
 <213> Homo sapien

<400> 261
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<210> 262
 <211> 587
 <212> DNA
 <213> Homo sapien

271

<400> 262
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<210> 263
 <211> 1413
 <212> DNA
 <213> Homo sapien

<400> 263
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272

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<210> 264

<211> 1533

<212> DNA

<213> Homo sapien

<400> 264

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273

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<211> 1693

<212> DNA

<213> Homo sapien

<400> 265

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274

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<210> 266

<211> 1715

<212> DNA

<213> Homo sapien

<400> 266

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<210> 267

<211> 1747

<212> DNA

<213> Homo sapien

<400> 267

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aagtggaaat atactatatg atacttttgt acgtgacttg tcttatttag tgtagtggtt 1680
tcaagggtcg tccatcatgt cgcataatc ctttattcct ttttatgggc aaataaattt 1740
cattgta 1747

```

```

<210> 268
<211> 665
<212> DNA
<213> Homo sapien

```

```

<400> 268
gggctggagg ccagaagcat agtatcgccc ttctctccag cctcagtcag agggacctcc 60
tgaggcctcc tctccaagtc ccttctccca caagcctagc catggacctg gcttgaacaa 120
ggccatggca gatacagtca gttttgcccc ctccacatct cccatctccc tcttcttcta 180
tgagtgcctc ccttctccca ctccctatgc acctgtgggg ttccaccact ttgccctctt 240
tgtgcagaaa ggggtgccag gcctgggtcaa gcagggcct ccctccttct gcctatagcg 300
attgggtcag ggatgagcac atggctggca gaactgggta aaagaagatt ttattccact 360
ggcctgaaag ctagcagggc atgagcctgg aactgctgcc agctatatta ttatctcata 420
aggagatcct atttgagggc taagccagca cagagcaagc acagttgagg gacaaagata 480
gagtgcctat ttagtgatct tagtgatcag cccgtggatc aagccatgcc tgaagcctaa 540
cccagccttt ccagaaacat gagtccataa agtttttttt gttttttgct taagcccatt 600
tcagttggac tttctgtccc ttgcaccagc ttttgccttg ctctctgcc acagacacag 660
ggccc 665

```

```

<210> 269
<211> 385

```

277

<212> DNA

<213> Homo sapien

<400> 269

```

ccctccttct gcctatagcg attgggtcag ggatgagcac atggctggca gaactgggta      60
aaagaagatt ttattccact ggcctgaaag ctagcagggc atgagcctgg aactgctgcc      120
agctatatta ttatctcata aggagatcct atttgagggc taagccagca cagagcaagc      180
acagttgagg gacaaagata gagtgcctatc ttagtgatct tagtgatcag cccgtggatc      240
aagccatgcc tgaagcctaa ccagccttt ccagaaacat gagtccataa agtttttttt      300
gttttttgct taagcccatt tcagttggac tttctgtccc ttgcaccagc ttttgccctg      360
ctcctctgcc acagacacag ggccc                                     385

```

<210> 270

<211> 733

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (502)..(520)

<223> n=a,c,g or t

<400> 270

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tttatcacca tgtcgtggct ttaacaacca atgccctatt ttccactgga aataaagtca      60
atagtgcctt taaactaaaa aagatgagaa atccaatttg agaaaacaca gaattgattt      120
agaaaactca ttcttaagat tctcttcttc tagaaccact tctggaacaa aatatctttt      180
ggtcagcggt gaaacggagt aacaaaatca atatgacata taaaaatgat ttattgcaag      240
gaactttctt atgccactgt gggactggct aagcaactgc aaaaaacata tggctatacc      300
ccaggatggc tcagatggaa cactaaccga cgagaggaag atgctactaa aagggtgcaat      360
ttcttttttc aaagaagctt cagctctact tttaaataat ttcaagtgat tcatcaggcc      420
cactgacatt atctcacata atatccctac tcaaagccaa ctgattatgg gctaaatatc      480
tacaaaatgc cttccatata gnnnnnnnnn nnnnnnnnnn tactgtttga ttaaataact      540
agggactgta gtctaggcat gttgtaatta aaattgatac cacacagatc ctcacatca      600
gaaaactggt taaggaaaaa ttaatatcca gtacaccagg atacagcagg cattagaaat      660
gaggttggag gtcaacttat ttatacagcc tttaacatta gtgtcatatt aggacaatcc      720
tgtaggagc aag                                              733

```

<210> 271

<211> 475

<212> DNA

278

<213> Homo sapien

<400> 271

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tttatcacca tgcgtggct ttaacaacca atgccctatt ttccactgga aataaagtca      60
atagtgcctt taaactaaaa aagatgagaa atccaatttg agaaaacaca gaattgattt    120
agaaaactca ttcttaagat tctcttcttc tagaaccact tctggaacaa aatatctttt    180
ggtcagcggt gaaacggagt aacaaaatca atatgacata taaaaatgat ttattgcaag    240
gaactttctt atgccactgt gggactggct aagcaactgc aaaaaacata tggctataacc   300
ccaggatggc tcagatggaa cactaacca cgagaggaag atgctactaa aaggtgcaat    360
ttcttttttc aaagaagctt cagctctact tttaaataat ttcaagtgat tcatcaggcc    420
cactgacatt atctcacata atatccctac tcaaagccaa ctgattatgg gctaa      475

```

<210> 272

<211> 403

<212> DNA

<213> Homo sapien

<400> 272

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ctttgtttct tgtgaccatg tatttttgca tattaagttc cgaatgtatg aatgcattta      60
ttcaactagt ctactccact ttcacatctt aaaataactc ttgttgtttt atttcactat    120
aaaagttgca aatgttcatt gaatataatg tgcaaatgtg gaaaaatata aaggaaattc    180
atcaaaatgt atcttaattt tataagtgat cttttccttc tgtttttcca ggcttttagt    240
caaattttta aatgagtttt cctcttatca tgaacattc tttaaaacta ttttggtatg    300
taattatfff gttgtacagt ttatatactg ttgaaaataa attttcctct gggatcttag    360
tttcttcag tttttcacca tgataaaaat aatattagta gag      403

```

<210> 273

<211> 403

<212> DNA

<213> Homo sapien

<400> 273

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ctttgtttct tgtgaccatg tatttttgca tattaagttc cgaatgtatg aatgcattta      60
ttcaactagt ctactccact ttcacatctt aaaataactc ttgttgtttt atttcactat    120
aaaagttgca aatgttcatt gaatataatg tgcaaatgtg gaaaaatata aaggaaattc    180
atcaaaatgt atcttaattt tataagtgat cttttccttc tgtttttcca ggcttttagt    240
caaattttta aatgagtttt cctcttatca tgaacattc tttaaaacta ttttggtatg    300
taattatfff gttgtacagt ttatatactg ttgaaaataa attttcctct gggatcttag    360
tttcttcag tttttcacca tgataaaaat aatattagta gag      403

```

279

<210> 274
 <211> 478
 <212> DNA
 <213> Homo sapien

<400> 274
 gtgatagaaa ctttcagctg aggagtctat atgccatact actctatgtg gcatctttag 60
 gtctctgtga aatcatgttg atgtaattga ttaacaaaaa taatttagaa aatacgtcag 120
 gcacagttga tggcttctca atatctgctt tgcattttta aacaaatcaa gaatgtaatt 180
 ttaacttttg cttatgggtca ttcttatgac tacacggaaa gggatggaat catacttact 240
 tgtcttatac atggactggt tttagttaac aataacataa ctacacaaag gaaaggaaat 300
 gtttacattt taaaaaatta ctgtaatta catctggtat ttttcagatt atgcataaaa 360
 taatatgagt ttgactattg tatcagaata ttttaaatcaa atcctgcaat ttatattaac 420
 ttaaaaaaac atctggtaaa gactgggtgt ggcagctcac gcctgtaatc ccagcact 478

<210> 275
 <211> 1109
 <212> DNA
 <213> Homo sapien

<400> 275
 taatacgacc acatagggat ttggccctca gcgagaattc ggcagagtgg gggttttgcca 60
 cgttggccag gctggtctca aactcctgaa ctcaagtaat ttgcctgctt cggcctccca 120
 gagtcctggg attacagtgc tgagccatcg cgcctggccg tgatagaaac tttcagctga 180
 ggagtctata tgccatacta ctctatgtgg catcttttagg tctctgtgaa atcatgttga 240
 tgtaattgat taacaaaaat aatttagaaa atacgtcagg cacagttgat ggcttctcaa 300
 tatctgcttt gcatttttaa acaaatacag aatgtaattt taacttttgc ttatgggtcat 360
 tcttatgact acacggaaag ggatggaatc atacttactt gtcttataca tggactgttt 420
 ttagttaaca ataacataac tacacaaagg aaaggaaatg tttacatttt aaaaaattac 480
 tgtcaattac atctggtatt tttcagatta tgcataaaat aatatgagtt tgactattgt 540
 atcagaatat tttaatcaaa tcctgcaatt tatattaact taaaaaaca tctggtaaag 600
 actgggtgtg gcagctcacg cctgtaatcc cagcactttg ggaggccgag gctggatgga 660
 tgattgcttg agcgcaggag ttctagacca gcctgggcaa tacagggaga cctgtctct 720
 atttcaaaaa taaataaata ggccccggtg tgtgatgttc ccttcctgt gtccatgtgt 780
 tctcaaaaaa aaaaaaaaaa taaaaataaa aataaataaa taaataaccg gtaaagatgt 840
 actgtttcta ctgcagtta taatatttca tttattaaga aagatatcat ctacagctttc 900
 aaattcaaca tagccctcaa tttatgacat aagttttata cttagtattt tataatttct 960

280

taatttttgtt ataaacttga aaatgtagaa tatgggggtcc aaaatctgtt gaacatttgt 1020
 tcagctagtt aggtttcaac attaatcata tacattaata gtatcttcat gtacgctatg 1080
 tgaaggggtgt tttttataag aaataggaa 1109

<210> 276
 <211> 1174
 <212> DNA
 <213> Homo sapien

<400> 276
 tgggggtttg ccacgttggc caagctgggc tcaaactcct gaactcaagt aatttgcctg 60
 cttcggcctc ccagagtcct gggattacag tcgtgagcca tcgcgcctgg ccgtgataga 120
 aactttcagc tgaggagtct atatgccata ctactctatg tggcatcttt aggtctctgt 180
 gaaatcatgt tgatgtaatt gattaacaaa aataatttag aaaatacgtc aggcacagtt 240
 gatggcttct caatatctgc tttgcatttt taaacaaatc aagaatgtaa ttttaacttt 300
 tgcttatggc cattcttatg actacacgga aagggatgga atcactactta cttgtcttat 360
 acatggactg ttttttagtta acaataacat aactacacaa aggaaaggaa atgtttacat 420
 tttaaaaaat tactgtcaat tacatctggc atttttcaga ttatgcataa aataatatga 480
 gtttgactat tgtatcagaa tattttaatc aaatcctgca atttatatta acttaaaaaa 540
 acatctggta aagactgggt gtggcagctc acacctgtaa tcccagcact ttgggaggcc 600
 gaggcctggat ggatgattgc ttgagcgcag gagttctaga ccagcctggg caatacaggg 660
 agaccctgtc tctatttcaa aaataaataa ataggccccg gtgtgtgatg ttcccccttc 720
 tgtgtccatg tgttctcaa aaaaattaaa aaataaaaaat aaaaataaat aaataaataa 780
 ccagtaaaga tgtactgttt ctactgcagt ttataatatt tcatttatta agaaagatat 840
 catctcagct ttcaaattca acatagccct caatttatga cataagtttt atacttagta 900
 ttttataatt tcttaatttt gttataaact tgaaaatgta gaatatgggg tccaaaatct 960
 gttgaacatt tgttcagcta gttaggtttc aacattaatc atatacatta atagtatctt 1020
 tatgtaagga tatgtgaagg gtgtttttct ttataagaaa attagtttaa tcaggtgagc 1080
 tgatacttag gattatacat atatctatga taaaattgaa agtaattgtg gttgttcttt 1140
 agagaacgtg ttttgatttt gacttagtat tggg 1174

<210> 277
 <211> 525
 <212> DNA
 <213> Homo sapien

<400> 277

281

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tttcattggt actagaatgt catctttcgc cgacaagttg ttccccagca gaatcctgct      60
gctcctggca caaaacaagc agatgaagag gtaaataacc ttgtgcaa atcttctcgg      120
cgctgagcct gccgcgcct aagcgcgctg ttattctagc ttatccgcaa ggactctgct      180
aaattaggca ggatgacatg tgggtgttct ccgttaaagc agatgggtac aatgaggctc      240
agagagatga gatgatttgg caggtaaatg agagcactag gctggcactc ggatcggcct      300
gctcccagtg gagggctttc tgccacccat gagccagcca tgtaaaatga gcaggggtgg      360
gttgatgag tgaatccctt aaggagcttg taaggatgca gatcaccgg ccctggagat      420
cctgagtctg ggaaacagtg gattggtgga ttctaagga ccttttagagg ctcaagatta      480
tccactgtgc ccagcctcag atctcacagg gccgggtatc tctttt                    525

```

<210> 278

<211> 402

<212> DNA

<213> Homo sapien

<400> 278

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gcggccgctg ggagcggggg tcgatcccgat gatgccgtcg tgggtgccgg ccagagaaga      60
gctccggagg ccggggcggc cggcgggctg gcgaatgtca tctttcccaa caagttgttc      120
ccagcagaat cctctctcct ggcacaaaac aagcagatga agagcagccc tgagaggtag      180
acacagcgga gatttttttc acccgcatctg tacagaagag aaaatgaagc ttgcccac      240
ctgcaggaga tcccctcacc ttgcaaaaga gccaaactgt ggctaaactg ggatcttcag      300
tccctggacc atttagcttg actaagagaa caggaaatgga ggccaaaaga tctacaaaat      360
gctcacacag agaagatgac agcttctaca aataaatgtc aa                        402

```

<210> 279

<211> 583

<212> DNA

<213> Homo sapien

<400> 279

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gcggccgctg ggagcggggg tcgatcccgat gatgccgtcg tgggtgccgg ccagagaaga      60
gctccggagg ccggggcggc cggcgggctg gcgaatgtca tctttcccaa caagttgttc      120
ccagcagaat cctctctcct ggcacaaaac aagcagatga agaggtaaat gaccttgtgc      180
aaatctcttc tcccgtgag cctgcccccc aaccctgtt attctagcta tcccaggac      240
tctgcaaatt aggcaggatg acagtgggtg ttcccgttaa acagatggga acaatgaggc      300
tcagagagat gagatgattt ggcagggtta tgagagccta ggctggcact cggatcggcc      360
tgctcccagt ggagggcttt ctgccacca tgagccagcc tgtaaaatga gcaggggtgg      420
gttgatgag tgaatccctt aaggagcttg taaggatgca gatcaccgg ccctggagat      480

```


282

cctgagtctg ggaaacagtg gattggtgga ttcctaagga ccttttagagg ctcaagatta 540
 tccactgtgc ccagcctcag atctccaggc cgggtatctc ttt 583

<210> 280
 <211> 781
 <212> DNA
 <213> Homo sapien

<400> 280
 ggggttaggg gcctgaagat ctggtgtctg atgtttgcag agcccaaccc tggaagaatg 60
 ccaggcacct ggcgaggaag ccatggtctc ttccttcctt gacttagaac aactaggagg 120
 ctctaggtt cagtcttact gggaagggga tgggaatgtg ggccaaagga cagggcagag 180
 gctgatctaa atacgtgggc cagctccact gaggaaactg agatggacca gtgtggcgtg 240
 gaagaaacca aggggagcag ccaaagtgtc tcttctccag gctgcctggc acagagctgg 300
 gcacacaacc aaccctgcag accagctgtc caatgggcaa gggaaggagc aaggcaggtc 360
 catctgcagt ctcggtctgt gggaaggtga gacagtgcag ggcataggag gctgactcca 420
 cagtggacag agaagacttt caggagatc agctcagctc agtctgaggg gcagggacag 480
 gaggagatag cgtttctgcg gttatcagga agggaagtgg aggaggcagc caggaagata 540
 tcgggaagaa agaggaaggg cgtgtgctag atcccgaaga ggaaaaagca gctgaattta 600
 gcagcctcag ggggtgtgaag gtcaaaagta tcaaggaatc ttaagcccag ggttctgggc 660
 caagaaagca gcactctctc tcatttacat gggcatctga gatgaaacct ggtgtccggg 720
 gacttctacc aacctaggat tcgtggggga gggcagtggt actggttcag aacgtggctc 780
 a 781

<210> 281
 <211> 1253
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (755)..(870)
 <223> n=a,c,g or t

<400> 281
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 ccaggcacct ggcgaggaag ccatggtctc ttccttcctt gacttagaac aactaggagg 120
 ctctaggtt cagtcttact gggaagggga tgggaatgtg ggccaaagga cagggcagag 180
 gctgatctaa atacgtgggc cagctccact gaggaaactg agatggacca gtgtggcgtg 240

283

```

gaagaaacca aggggagcag ccaaagtcc tcttctccag gctgcctggc acagagctgg 300
gcacacaacc aaccctgcag accagctgtc caatgggcaa ggggaaggagc aaggcaggtc 360
catctgcagt ctcggtgct ggggaaggtga gacagtgcag ggcattggag gctgactcca 420
cagtggacag agaagacttt caggagatc agctcagctc agtctgaggg gcagggacag 480
gaggagatag cgtttctgcg gttatcagga aggggaagtgg aggaggcagc caggaagata 540
tcgggaagaa agaggaaggg cgtgtgctag atcccgaaga ggaaaaagca gctgaattta 600
gcagcctcag ggggtgtgaag gtcaaaagta tcaaggaatc ttaagcccag gggtctgggc 660
caagaaagca gcactctctc tcatttacat gggcatctga gatgaaacct ggtgtccggg 720
gacttctacc aacctaggat tcgtggggga gggcnnnnnn nnnnnnnnnn nnnnnnnnnn 780
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 840
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn tatagggttg ctctaaagat tagacaaggc 900
caagtgttca gaacaatact ggcataatac aagagctcca aaattttatt tttcagttac 960
tttgctccaa tcgggtaact ccaggagag tgtcacagag caggacagca aggacagcac 1020
ctacagcctc agcagcaccg tgacgtgag caaagcagac tacgagaaac acaaagtcta 1080
cgctgcgaa gtcacccatc agggcctgag ctgcccgtc acaaagagct tcaacagggg 1140
agagtgttag agggagaagt gccccacct gtcctcagt tccagcctga cccctccca 1200
tcctttggcc tctgaccctt tttccaaggg gacctacccc tattgcggtc ctc 1253

```

<210> 282

<211> 781

<212> DNA

<213> Homo sapien

<400> 282

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ggggttaggg gcctgaagat ctggtgtctg atgtttgcag agcccaaccc tggaagaatg 60
ccaggcacct ggcgaggaag ccatggtctc ttccttcctt gacttagaac aactaggagg 120
ctcctaggtt cagtcttact ggggaagggga tgggaatgtg ggccaaagga cagggcagag 180
gctgatctaa atacgtgggc cagctccact gaggaaactg agatggacca gtgtggcgtg 240
gaagaaacca aggggagcag ccaaagtcc tcttctccag gctgcctggc acagagctgg 300
gcacacaacc aaccctgcag accagctgtc caatgggcaa ggggaaggagc aaggcaggtc 360
catctgcagt ctcggtgct ggggaaggtga gacagtgcag ggcattggag gctgactcca 420
cagtggacag agaagacttt caggagatc agctcagctc agtctgaggg gcagggacag 480
gaggagatag cgtttctgcg gttatcagga aggggaagtgg aggaggcagc caggaagata 540
tcgggaagaa agaggaaggg cgtgtgctag atcccgaaga ggaaaaagca gctgaattta 600

```

284

gcagcctcag ggggtgtgaag gtcaaaagta tcaaggaatc ttaagcccag ggttctgggc 660
 caagaaagca gcactctctc tcatttacat gggcatctga gatgaaacct ggtgtccggg 720
 gacttctacc aacctaggat tcgtggggga gggcagtggg actgggttcag aacctggctc 780
 c 781

<210> 283
 <211> 969
 <212> DNA
 <213> Homo sapien

<400> 283
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 tctccagacc ctacctctgc ccagtgctag gaggaatttc ctgacgcccc ttctcttcac 120
 ccatttcctt tttagcctgg agagaagccc ctgtcaccce gtttattttc atttctctct 180
 gcggagaaga tccatctaac ccctttcttg cccagagtc cagggaaagg atgatcactg 240
 tcagaagtcg tggcgcgggg gccactggg cgctttgtca cattccaccg aaagtcccg 300
 cttgggtgaca gtgtgcttcc ctccctcgc caacagttcc gagtgagctg tgcttttagct 360
 ctctgtggggg tgggtcaagg gaggatttga agagtcattg cccacttta cccttttgga 420
 gaaatggctt gaaatttgct gtgacacggg cagcatggga atagtccttc ctgaaccctg 480
 gaaaggagct cctgccagcc ttgcacacac tttgtcctgg tgaaaggcag ccctggagca 540
 ggtgtttttt tggaaactcca aacctgcca cccaacttgc ttctgaaagg gactctaaag 600
 ggtccctttc cgctcctctc tgacgccttc cctcagccag aattcccttg gagaggaggc 660
 aagaggaaag ccatggacag gggtcgctgc taacaccgca agttcctcag accctggcac 720
 aaaggccttg gctacaggcc tccaagtagg gaggaggggg aggagtggct gcctggccac 780
 agtgtgacct tcagaggccc ccagagaagg acacctggcc cctgcctgcc tagaaccgcc 840
 cctcctgtgc ccctggcct tgggaagggg atgaaatttc cgtcccctt cctccttggg 900
 gcccaggagg agtggagggt cccgggagaa tattgtcagg ggaaggcag ggggtgtcat 960
 gggaatgcg 969

<210> 284
 <211> 313
 <212> DNA
 <213> Homo sapien

<400> 284
 aattcacaga aagagctaga gtgtcgaggt agaggtagca attttaaatg gagatgttag 60
 ggaaatcctc actgagaagg taacatttgg tgaaaaaaaa aaaaagtggc aagcaaggga 120
 accatccaga tagggggcctt gtaggtggtg ggagatacgt gggatgaatt gggacacttt 180

285

gagttgcatg tttgagaagt aatatgaagg cagagagcgg ataggagctg cggaacagat 240
 ggaccaaagt gacgggcaag atgccgcaa cacaggcagg ggcgggggca gactgagggg 300
 gaagtgagta gca 313

<210> 285
 <211> 1243
 <212> DNA
 <213> Homo sapien

<400> 285
 aggtgtagct tgactcataa catcactaac cctactacca atggatgatgt gtaagcactt 60
 tgtgctgggt taaagtttca aacattttct tatagagatt agatgatcta agcagtagag 120
 tcccttaaat caaggttcag ggccaggcgc ggtggctcac gcctgtaatc ccagcacttt 180
 aggaggccga ggtgggaggga tcacgaggtc aggagatcga gacaaccccg tctctactaa 240
 aaaaaatgca aaacgttagc tgggcatggg ggtgggcgcc tgtagtccca gctactaggg 300
 aggctgagac aggagaatgg cgtgaacccg ggaggcggag cttgcagtaa gccgagatcg 360
 cgccactgca ctccagccta ggcgagagag cgagactccg tctcaaaaaa aaaaaaatg 420
 agctgagcgt ggtggcatat gcctgtaatc ccagctactc tagaggccga ggcaggagaa 480
 ttgcttgagc ccggaagggt gaggttacag tgagccaaga ttgtgccact gcaactccagc 540
 ctgggtgaca aagactctgt ctcaaaaaa aaaaaaatat atagtaagtg caatggagaa 600
 aataattcac agaaagagct agagtgtcga ggtagaggta gcaattttta atggagatgt 660
 tagggaaatc ctactgaga aggtaacatt tggtgaaaaa aaaaaaagt ggcaagcaag 720
 ggaaccatcc agataggggg cttgtaggtg gtgggagata cgtgggatga attgggacac 780
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293

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294

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296

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298

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299

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300

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<210> 296

<211> 870

<212> DNA

<213> Homo sapien

<400> 296

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301

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<210> 297

<211> 1141

<212> DNA

<213> Homo sapien

<400> 297

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302

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<210> 298
 <211> 1140
 <212> DNA
 <213> Homo sapien

<400> 298
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<220>

303

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<400> 299
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<210> 300
 <211> 2069
 <212> DNA
 <213> Homo sapien

<400> 300
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304

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<210> 301

<211> 786

<212> DNA

<213> Homo sapien

<400> 301

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305

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<210> 302
<211> 1128
<212> DNA
<213> Homo sapien

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gatttgactg ctagtgtcct ctaacttctt cctctatcgc ctgtattcct tgcaaaggag 360
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aagactgtct ttggctttct aggactccat cccagggag gatcacctag ggagggattt 540
gtggttatat agagacaggg agagaaacag acccattttc cctcgctgtg aaaggatcaa 600
cactgaattt ggaatttagt ctggaagttg actattttta ttctctggac ttcaatttcc 660
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306

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| gcctggccaa | tttttgtgtt | tttttgcaga | gacaaggggt | tgccatgtta | cacatgcagc | 1020 |
| tcttgaactc | ctgggctcaa | gcctctgcct | gcctcagctt | catcaacgtg | ctgggattac | 1080 |
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 <211> 432
 <212> DNA
 <213> Homo sapien

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| aatgagaaga | ttggtaggaa gggcggtttc ttgctgtgtc caagaacagg aattgagaaa 180 |
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| gaaacaaagt | ataccacaag gaatgggaac atgtagagct gttttaaaaa tgtttctgtg 300 |
| tttgtgtgag | tctgtgtact agatatattt ttaaaatgac ttttctcgga attacatcat 360 |
| actttgaaga | tcagcatagg aagtaatatg aatgggctca ctatagccaa gtgcacttag 420 |
| ttcccttgat | ct 432 |

<210> 304
 <211> 431
 <212> DNA
 <213> Homo sapien

| | |
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| gaaacaaagt | ataccacaag gaatgggaac atgtagagct gttttaaaaa tgtttctgtg 300 |
| tttgtgtgag | tctgtgtact agatatattt ttaaaatgac ttttctcgga attacatcat 360 |
| actttgaaga | tcagcatagg aataatatga atgggctcac tatagccaag tgcacttagt 420 |
| tccttgatc | t 431 |

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 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 305

307

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 cacaattgct ttatagttag gaaattatit taaactatat gtgtttttaa aatcagcaga 360
 gctaacaaca ttatacctag gg 382

<210> 306

<211> 452

<212> DNA

<213> Homo sapien

<400> 306

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<210> 307

<211> 708

<212> DNA

<213> Homo sapien

<400> 307

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308

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 <213> Homo sapien

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 <211> 816
 <212> DNA
 <213> Homo sapien

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309

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<212> DNA
<213> Homo sapien

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311

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315

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318

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319

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321

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322

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323

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324

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<212> DNA
<213> Homo sapien

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325

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326

<211> 2799

<212> DNA

<213> Homo sapien

<400> 319

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327

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<210> 320

<211> 1064

<212> DNA

<213> Homo sapien

<400> 320

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328

| | |
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| tgtaaagaaa cattttggac aaagagtgtg tacaatttaa gcaacattca aaggttgact | 660 |
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| atattttctt acgtgtatat atggtagcat gaagctttgt aatcattgtt ttgagagatt | 780 |
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| gcatggccag ctgacagtat cgtcagtggg cagaatgtat atagtgcata tatccttctt | 1020 |
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<210> 321

<211> 2383

<212> DNA

<213> Homo sapien

<400> 321

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| tcgggtggagc actgcggcac tcagcccgag ctgccgtttt cccctcgcgg ggaacgctgt | 180 |
| gacccccccg caggagcggc ggggcggggg gggggggccc gggagaagat ggcgacgccg | 240 |
| ggaagcgaac cccaaccttt cgtcccggcc ctttcggtag ctactctgca cccacttcat | 300 |
| catccccacc accaccacca ccaccatcag caccacggag gaaccggcgc ccccggcggg | 360 |
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| cttaatctgt atcacaactg tatcagagtc attcctgagg ccatcgtaa tctgcagatg | 660 |
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| gttttaccac aagaactagt agatcttccc ttggtaaagt ttgacttttc ctgcaacaaa | 960 |
| gtgctcgtga ttccaatttg ttttagagag atgaagcagc tgcaagtgtt actacttgag | 1020 |

329

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<211> 1675

<212> DNA

<213> Homo sapien

<400> 322

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330

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<210> 323

<211> 4713

<212> DNA

<213> Homo sapien

<400> 323

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331

| | |
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| catccccacc accaccacca ccaccatcag caccacggag gaaccggcgc ccccggcggg | 360 |
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| ccgcagttta caatccggag gaaaatggag cagatgagag aagagaaaga gctggtggaa | 1980 |
| caacttcgtg agagcattga gatgagattg aaggctcagtc tacacgaaga cctgggggca | 2040 |

| | |
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333

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334

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335

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337

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338

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<211> 2785

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341

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 <213> Homo sapien

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342

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 <212> DNA
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343

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 <211> 1136
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 <213> Homo sapien

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344

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<211> 1565

<212> DNA

<213> Homo sapien

<400> 333

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<211> 1749

<212> DNA

<213> Homo sapien

<400> 334

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346

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<211> 1815

<212> DNA

<213> Homo sapien

<400> 335

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347

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<211> 2132

<212> DNA

<213> Homo sapien

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 tgaaatgtgc ttgcccttca tccctaaggc ctgcgtccct tcctcagaga ggactaagcc 780
 cctctcccag tcttgatgtt ctccgaggcc cttcttattc acagaacctt tctggcttat 840
 ttattcgctt gcttgcttct gatgtcttct ctactgaaa ggaatcgaag ggccaaggaa 900

348

| | |
|--|------|
| tgtgtttttc gttgatgtca gcttgctgca aaggaccaca cctgcttctc gaccaggaa | 960 |
| cgtgggaaag ggaaaggctt ggcttgtttt ggtggagatg gagatgctgg taacagtggg | 1020 |
| ggaatgccct ccttctgatt cacagtgggg aggtgctctg ggcccctgcc actgcccagag | 1080 |
| gacttcaggt aagtcagccc gtggccccc gcccttccct gccagacgcc ctggcagacg | 1140 |
| gcttgttctg acaagtatgc gctttctgga tggaacagcc tcccttttgt ccaaaccctt | 1200 |
| cctttgaatt taaaatgcac aaagaacctt tcgaagagga aaagaatggg atcaggaaga | 1260 |
| ggaggctgta tctcatttgg aactcaagc cctcagctcc tgccaagag tttctgtaat | 1320 |
| ttgctccac atcacgtcat gacttttggc tcccagccag gtgcggtggc atctgtggct | 1380 |
| tcaccttctt gggaagtcag ggtcatgttc ccttgagtct tctcccttct ctctccccag | 1440 |
| cttttggttg tcctgctgag aggatgcggc atttgagcag tagcttctgg agcccagagt | 1500 |
| gaagccccac ccaggcacc tgacaggacc acaggaatgc tcctggcaca gcaagcagga | 1560 |
| ctcttgagaa gctcagcctc cacgctcctt gtagatgttc agttcaaact ccacagtttg | 1620 |
| tgtgactcac tgaagggtt gggttggctc tcgctgacga gtctgtcatc ggtgccaggt | 1680 |
| gacacgcttt tcccctcctc ccgtctagtc ctctctcttg cccagggtt tctggtggg | 1740 |
| aagtttaacc tcctcttcat aagcagtggg agggctactg tgctgccctc tggccaagc | 1800 |
| tctggtattc cctttgcagt ggtgggtgct ctcatcctt tgcagtgtgc ctgcagtgtg | 1860 |
| aaccaggggg atccacgaga cagggaactc acgtctgttt tcttcatttg gtgtagcatg | 1920 |
| ccattgggcg ttgcccagac agggcctatc atgtgggtcc tacacctatt cacacacctg | 1980 |
| ccatttgctt tcagaatcct gttcccagtg ggtaatgggt taaaagccc atagctgagt | 2040 |
| ttatccacat tggatccgac ccacattcca tgctcttgta agtctccagt tggtaaagt | 2100 |
| agcagtttga tcccttgatc cttcaaaata ct | 2132 |

<210> 337

<211> 1132

<212> DNA

<213> Homo sapien

<400> 337

| | |
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| gcaaagggtcc tcctgggtgc catcgccagt gcggggcagc ctgcgagccc cttgaggggag | 120 |
| gtctccctca accsmacwcc tcctggggcc gagcaggagt cacatccaag ggctgggtca | 180 |
| ttatctgata aatgagtggg ttgtgaggat gagtaaacag ggactgacct agaggtcagg | 240 |
| tgtaactcag cctcagaaac kgcgtgtgtc aataggaatc gaagggccaa ggaatgtgtt | 300 |
| tttcgttgat gtcagcttgc tgcaaaggac cacacctgct tctcgaccca ggaacgtggg | 360 |

349

aaagggaaag gcttggcttg ttttgggtga gatggagatg ctggtaacag tggaggaatg 420
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 aggtaagtca gcccggtggc cccagccctt ccctgccaga cgccctggca gacggcttgt 540
 tctgacaagt atgcgctttc tggatggaac agcctccctt ttgtccaaac ccttcctttg 600
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 tgtatctcat ttggacactc aagccctcag ctctgcccc agagtttctg taatttgctc 720
 ccacatcacg tcatgacttt tggctcccag ccagcttttg gttgtcctgc tgagaggatg 780
 cggcatttga gcagtagctt ctggagccca gagtgaagcc ccaccaggc accctgacag 840
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 ccttgtagat gttcagttca aactccacag tttgtgtgac tctactgaagg gcttgggttg 960
 gctctcgctg acgagttctg catcggtgcc agacaaccgg gtttcaccgt gttagccagg 1020
 ctggcctcaa actcctgacc tcaagtgatc caccgcctc gacctcaca agtgcttggg 1080
 ttacaggtgt aagctactgt gccaggccag aaaaaataaa ataaaaataaa at 1132

<210> 338

<211> 1454

<212> DNA

<213> Homo sapien

<400> 338

gaaataaatg aagaggaggc gggggtcagg aggggcatgt tttatatgag tagataccat 60
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 gtctccctca accsmacwcc tcctggggcc gagcaggagt cacatccaag ggctgggtca 180
 ttatctgata aatgagtggg ttgtgcggat gagtaaacag ggactgaccc agaggtcagg 240
 tgtaactcag cctcagaaac kgcgtgtgtc aataggaatc gaagggccaa ggaatgtgtt 300
 tttcgttgat gtcagcttgc tgcaaaggac cacacctgct tctcgaccca ggaacgtggg 360
 aaagggaaag gcttggcttg ttttgggtga gatggagatg ctggtaacag tggaggaatg 420
 ccctccttct gattcacagt ggggaggtgc tctgggcccc tgccactgcc cgaggacttc 480
 aggtaagtca gcccggtggc cccagccctt ccctgccaga cgccctggca gacggcttgt 540
 tctgacaagt atgcgctttc tggatggaac agcctccctt ttgtccaaac ccttcctttg 600
 aatttaaaat gcacaaagaa cctttcgaag aggaaaagaa tgggatcagg aagaggaggc 660
 tgtatctcat ttggacactc aagccctctt ttggttgtcc tgctgagagg atgcggcatt 720
 tgagcagtag cttctggagc ccagagtga gccccacca ggcaccctga caggaccaca 780
 ggaatgctcc tggcacagca agcaggactc ttgagaagct cagcctccac gtccttgta 840

350

```

gatgttcagt tcaaactcca cagtttgtgt gactcactga agggcttggg ttggctctcg      900
ctgacgagtc tgtcatcggg gccaggagct gagaacagcc cccttcctat ttgaggctgg      960
cctgtccatg cgcacccttg gcctcacatc aatggaggat caccatccc ttctctgtgc     1020
tagaaacca atggctgtat tccataagcc tgcaggactc ttgtcttctt ccttatttaa     1080
ctacaccagc ttaggagtag cctacatgct ccatcttcat ttcttacctc catctactcc     1140
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cacactcact tgtccagggt cacattaata cctacacctg actatcctac agataactcg     1260
aattcaagat ggtgggggaa taaactcacc atcttactct atatgtctgc ctgtccttca     1320
gtattttctca tgtgggataa ggggtgctatg attcaccac ttgtccaaga cagaacacct     1380
cgatgtcatt ctttttttaa atttttaatt tttttttgag acagagtttc gctgttatca     1440
cccaggctgg agtg                                     1454

```

<210> 339
 <211> 596
 <212> DNA
 <213> Homo sapien

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<400> 339
tgtttccctt ggtctctact tccctgattc cctcctctcc taactgtctt tctcttcttc      60
tctccaggag ctgagaacag ccccttcctt atttgaggct ggctgtcca tgcgcacctt     120
tggcctcaca tcaatggagg atcaccatc ccttctctgt gctagaaacc caatggctgt      180
attccataag cctgcaggac tcttgtctct ctccttattt aactacacca gcttaggagt      240
agcctacatg ctccatcttc atttctctac cccatctact ccacagtcta ccattctctt     300
gctgagggtta ctacactggc ctctttctct tacactcttt tccacactca cttgtccagg     360
tgcacattaa tacctacacc tgactatcct acagataact cgaattcaag atgggtggggg     420
aataaaactca ccactctact ctatatgtct gcctgtcctt cagtatttct catgtgggat     480
aagggtgcta tgattcacc ccttgtccaa gacagaacac ctogatgtca ttcttttttt     540
aaatttttaa tttttttttg agacagagtt tcgctgttat caccaggct ggagtg         596

```

<210> 340
 <211> 1467
 <212> DNA
 <213> Homo sapien

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<400> 340
gaaataaatg aagaggaggc ggggggtcagg aggggcatgt tttatatgag tagataccat      60
gcaaagggtc tcctgggtgc catcgccagt gcggggcagc ctgcgagccc cttgaggggag     120
gtctccctca accsmacwcc tcctgggggc gagcaggagt cacatccaag ggctgggtca     180

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351

```

ttatctgata aatgagtggg ttgtgcggat gagtaaacag ggactgaccc agaggtcagg 240
tgtaactcag cctcagaaac kgcgtgtgtc aataggaatc gaagggccaa ggaatgtgtt 300
tttcgttgat gtcagcttgc tgcaaaggac cacacctgct tctcgaccca ggaacgtggg 360
aaagggaaag gcttggcttg ttttgggtga gatggagatg ctggtaacag tggaggaatg 420
ccctccttct gattcacagt ggggaggtgc tctgggcccc tgccactgcc cgaggacttc 480
aggtaatgca gcccgaggcc ccagccctt ccctgccaga cgccctggca gacggcttgt 540
tctgacaagt atgcgcttct tggatggaac agcctccctt ttgtccaaac ccttcctttg 600
aatttaaaat gcacaaagaa cctttcgaag aggcagctcc tgcccaagag tttctgtaat 660
ttgctcccac atcacgtcat gacttttggc tccagccag cttttggttg tcctgctgag 720
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ctacactctt ttccacactc acttgtccag gtgcacatta atacctacac ctgactatcc 1260
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tgctgtcct tcagtatttc tcatgtggga taagggtgct atgattcacc cacttgtcca 1380
agacagaaca cctcgatgtc attctttttt taaattttta attttttttt gagacagagt 1440
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<210> 341
<211> 467
<212> DNA
<213> Homo sapien

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```

<220>
<221> misc_feature
<222> (166)..(166)
<223> n=a,c,g or t

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<400> 341
caggaagacc ctctcagaaa aaaaaaaaaa agaatttggc cgttatgtgg aggactggaa 60
ttgagaaggg caagagcgag gtagaagagt ggtctagga gaacagttag gggctattgc 120

```

352

```

aattatccag caagagatct tggaccagga tggcagcagt ggaggnggta aaatgtgggt 180
ggatgaagcg tacgctttga aggtatcaac aggaccagct gatggaaggg agtcaacagg 240
actagctgat ggctgtaaac tgggggggtca ctagctatca gatggcattt acttaaagcc 300
atggaagtag gtgagctccc ttatggagag ggaataggaa ggaggtagac cattctatca 360
aaatgctctt tctacagggc acttctcact gagatattat ttatctggga tttatattat 420
ttattcaatt tgttttgtgt ttggttctat tagaaaagct ccatagg 467

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```

<210> 342
<211> 783
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (166)..(166)
<223> n=a,c,g or t

```

```

<220>
<221> misc_feature
<222> (506)..(607)
<223> n=a,c,g or t

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<400> 342
caggaagacc ctctcagaaa aaaaaaaaaa agaatttggc cgttatgtgg aggactggaa 60
ttgagaaggg caagagcgag gtagaagagt ggtctagggg gaacagttag gggctattgc 120
aattatccag caagagatct tggaccagga tggcagcagt ggaggnggta aaatgtgggt 180
ggatgaagcg tacgctttga aggtatcaac aggaccagct gatggaaggg agtcaacagg 240
actagctgat ggctgtaaac tgggggggtca ctagctatca gatggcattt acttaaagcc 300
atggaagtag gtgagctccc ttatggagag ggaataggaa ggaggtagac cattctatca 360
aaatgctctt tctacagggc acttctcact gagatattat ttatctggga tttatattat 420
ttattcaatt tgttttgtgt ttggttctat tagaaaagct ccatagggcc cgggcacggt 480
tggcttttgc ctgtaatccc aacacnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 540
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 600
nnnnnnntca gctccttctt tcattccaga cctgccccct ggagatcgct ccctgaatgc 660
ccctcagaca ccacaggctc ggcgagaaat tgatctcccc agcttttccc cagctctggc 720
cccatcgctg tttctcattt ccgtggacac ccacgccaga aacctggatc tcatccttgc 780
ctt 783

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353

<210> 343
 <211> 1305
 <212> DNA
 <213> Homo sapien

<400> 343
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 tatttagtag agtttttagg aagatgaaaa taatttcata aaatacttag aattgtagtg 120
 ggacagatta aattctgtat atgtgttttag aaaacatatt cattcatttg ttccacaact 180
 attcattgag tgctcacaca ctagacattg atttacggtc atggaataag tacatcagac 240
 aacaagtcaa gtcaagtctt tgctcatgg agctaacatt ctaagaggag aaacatgcag 300
 taaacaagta aagaaatgta tgctctattc agggagtagt ttgtgctatg aggaaaagca 360
 aaacagggtg aagagatagc tatgtgggtg gagtgggact atttcgtaca gggcactgat 420
 tgtagacctc tgatgagata acatttgaca agagatctgc agggagctat gtgtcatggg 480
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 ataatttggg ctgggcatgg tgggttcctgc ctgtaatccc agcactttgg gagggtgagg 600
 tgggcgaatc acttgaatct gggagttaga taccagttcg ggcaacatgg cgaaatcccg 660
 tctctacaaa aaatacaaaa attagccagt gtggtggcac gcgcctgcag tcccagctac 720
 ttgggaggct gaggtgggag aattgcttgg atctgggagg tggaggttgc agtgaactca 780
 gattgcgcca ctgcactcca gcctgagatt gtgccactgc actccagcca ctgcactcca 840
 ggaagaccct ctcaaaaaa aaaaaaaaaa aatttggccg ttatgtggag gactggaatt 900
 gagaagggca agagcgaggt agaagagtgg tctagggaga acagttaggg gctattgcaa 960
 ttatccagca agagatcttg gaccaggatg gcagcagtgg aggtggtaaa atgtgggttg 1020
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 tagctgatgg ctgtaaaactg gggggtcact agctatcaga tggcatttac ttaaagccat 1140
 ggaagtaggt gagctccctt atggagaggg aataggaagg aggtagacca ttctatcaaa 1200
 atgctctttc tacagggcac ttctcactga gatattattt atctgggatt tatattattt 1260
 attcaatttg ttttgtgttt ggttctatta gaaaagctcc atagg 1305

<210> 344
 <211> 253
 <212> DNA
 <213> Homo sapien

<400> 344
 atctggataa cctccatcaa tgtatttaac ctcatctta gttttctcat cggaaagcag 60
 ggatgatgat gataatgtga cgtcacacga ttgagaaagg ttataggtaa ccacacgtcc 120

354

tgaacaccca actcggaatc tggcccagca gacactcaga tatgagtccc caagtatttg 180
aatgtctact gtgagcctgg aactgtcctg gggactgtgg actcaacaga aaaccacacc 240
cctgcctcta gga 253

<210> 345
<211> 513
<212> DNA
<213> Homo sapien

<400> 345
atctggataa cctccatcaa tgtatttaac ctcatcttta gttttctcat cggaaagcag 60
ggatgatgat gataatgtga cgtcacacga ttgagaaagg ttataggtta ccacacgtcc 120
tgaacaccca actcggaatc tggcccagca gacactcaga tatgagtccc caagtatttg 180
aatgtctact gtgagcctgg aactgtcctg gggactgtgg actcaacaga aaaccacacc 240
cctgcctcta ggaggtttgc gttctagcgg gcacgggcga gaccagctat aaaccacata 300
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ctattctggg aggtatctgg tgacatttga gcagagactt gatgggccc ggtggtggct 420
atcactcgtg agagctttgg gcatcattcc tcccagcaca tgctccagtt acgtggagggc 480
aggactggca tttgggtgat tttcttgat tgc 513

<210> 346
<211> 353
<212> DNA
<213> Homo sapien

<400> 346
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ccattgcaat ttctcacatg gagttctact tcaaggaaga gctctttcct ctcccaacgt 120
gttttaggac cttaatacat aatgacaaat agttttataa atagctgtta atgtagtgtc 180
atccataatc tgtgaatatc agcacatgat atcatgtaag ttgctctttt tttggctaata 240
taaccgacaa aaagatgcac tgttgctgtt ttaatttgog tatctttaat tacaattaag 300
gctgaacttt aaaaaatata tttactgaat ttcactctct ctagctttca cat 353

<210> 347
<211> 2111
<212> DNA
<213> Homo sapien

<400> 347
caaagatgct tggagattga ttgatgttgt aaagtgcttt gatatctttc atagagtgtt 60
caataagagc aaaatatgtc atcagaactt agtctaaagc aaactagtcc caaaccgtct 120

355

| | |
|--|------|
| tgagtagata ctaagcgggt ttgtgtcttt gttataagtt gtacttatat tttcgagaga | 180 |
| aagtttttca tgttctgatt ttcttttaag tgtcagctgt atgtttgggg tctttacctg | 240 |
| ttaaacttgag ttccaacatg cttttagat ggtcagtcac ctacagagga caatttttct | 300 |
| agccaaggag ttaaateccac cttaaaatgc ttcttgccaa ggacaatgcc ttgcaata | 360 |
| tttgagatgt ttattctcag ttgtgattta ttactgaatc tgtgtcttca tagcgactcc | 420 |
| ttgggagggt caggaggagg cagagccaga aagcaagtcc ctgcaatcag ttcattatag | 480 |
| agaaagaaaa agcttttatt tcaggattct ggtggataga cttactgata tgtatattct | 540 |
| gtgtctattt aatttcacgt agtgctgcat ctaatcacgc tgtttaaata atcggacaga | 600 |
| atgtcctttt gctttgcttt tgcttgtaa gagcacacag cactgccacc ttgttgccaa | 660 |
| agtttggctc gatattgaat tgcttaaaaa tcaagtgaat gcctgttggg aaaaagctta | 720 |
| ctccttctct ttgtcagtac ttgcaaaaac aacttaaaag aagttagtat tattggactg | 780 |
| aattcagtaa ttagcataat catgatgcta tgtattgttc accagggcac gcccttggc | 840 |
| cgcatttccc attaagagga caccgatgtt gtcctagtga ataaatcccg gcacacatga | 900 |
| tgcaaatcag cgtgttcctg cctgctgctt ggctgcagtt aattttagcc ggggttagtt | 960 |
| ctatgagttg taaaagtaga agttagcaag ctgaaatgtg acttctcggc ctaatgtggt | 1020 |
| aggatatcta ttttagactt cagatttgtt ttgtgatcag gagagcagtc ttctgaagaa | 1080 |
| ttgtggctca gttttcttgg aaactacttg taagtactgg gtggaatfff aagacttctc | 1140 |
| tttgttcttt tctccttaaa tcttcctaatt gttaccgtca tagtaatgtt tatctcttgg | 1200 |
| gaaaactgga agctttcagg ttggtacgtt agagaaagct aagagagggt gcaaaagggt | 1260 |
| tttctttaaa tgtctcctac tgcaataaat ctgccttatt caatttgccc aagaaaaagt | 1320 |
| tttogatctt tacttatttt tgcaaaagca atctgtagat tattatftta tgttaaaata | 1380 |
| tttgattaat ggatatggtt tctgtaaata cagaaacatt gtattgtgtc attgagcttt | 1440 |
| gttttctact atggtaacct aattcttgag aaaaaaatgt tgaaagttaa ttctgttat | 1500 |
| actctgtgct acaagtttat tttgtagaaa taatggagtg tcaaatgtaa ttttcttgaa | 1560 |
| tgtatagatg gacagttttt tatcctttta agggggattt tgtgcttaaa aaataaacc | 1620 |
| atatatgcct aaagagaagc actttaaaaa attaatfttag gaagaagggt ttagagaata | 1680 |
| atttaaagca tctcttttta gactgagtta gttatcaaaa gtaaccaaag gccatgggat | 1740 |
| tctgtaacct taactgcagt tcatctaaca cattattacc aacttaaatt tgtactgaag | 1800 |
| aaaacaaaag attttgatat tgaatatttt aaattaaatt tgaatcatct tgcttattta | 1860 |
| gaagtgtgtt ttcaatgtgg actgacctca agccaaacag tttgcttaca gcagagaacc | 1920 |
| aggcaggaat ttctttatca attagcaagt aaatgtatca gctttaggaa tattgatatt | 1980 |

356

aataaaacag ttctcctagg cgataggata ggtgctcacc agctatctat gcctgtcatc 2040
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 gaaaagattt a 2111

<210> 348
 <211> 723
 <212> DNA
 <213> Homo sapien

<400> 348
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 ctgtatacag acaaactcac cagtctcaac aaagcgaaag tcactttgag atttttccta 360
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357

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358

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359

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<211> 1716

<212> DNA

<213> Homo sapien

<400> 352

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| taatgttgta ctagagcttg tttctgagat tagcccatgt acattggtag agtgtagcct | 180 |
| ttgtggctca cctgttttta ctttgcaatg tctgctccca cagggtgggct cgggtggtggc | 240 |
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360

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361

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365

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366

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367

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<213> Homo sapien

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371

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397

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403

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406

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411

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416

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| ctaaataata atgtgtcaga tgcctgtgag tggactgcct ggccaaatga ctcatgaaga | 780 |
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| cgagaccagc ctgaccaaca tgggtgaaacc cccgtctcca ctagaaatgc aaagattagc | 2100 |
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417

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418

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<211> 2720

<212> DNA

420

<213> Homo sapien

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| cccggcccga ctcccgggct cccgcgggtg ggggccaggg ctggtcggcg ccggcggggc | 180 |
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421

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<212> DNA

<213> Homo sapien

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422

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<211> 996

<212> DNA

<213> Homo sapien

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423

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424

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425

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<212> DNA
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428

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<211> 1026

<212> DNA

<213> Homo sapien

<400> 385

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430

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 <212> DNA

431

<213> Homo sapien

<400> 388

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<211> 276

<212> DNA

<213> Homo sapien

<400> 389

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<210> 390

<211> 276

<212> DNA

<213> Homo sapien

<400> 390

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<211> 303

<212> DNA

<213> Homo sapien

432

<400> 391
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 tcaacaagtt ggtggatgct gatgaaaggg gaagtagtaa atagcaaagg tctcaatgcc 120
 tgactctgag atggagtaag gatgagctat caggactggc acttcacttc taaatgttga 180
 gcactcaggt tttgctaaat ttataaaaagc acatgaacta actaacatcg catatttcct 240
 taacgagaaa accagtttat ctctgtttta aacagttctg atctactcaa atacacattt 300
 tta 303

<210> 392
 <211> 994
 <212> DNA
 <213> Homo sapien

<400> 392
 gggggagatt tgaactcaga tttgtgcaat tctaaagcca gcctgtttat tatagtctcc 60
 caggagacaa caacagaaac aatgagaaaa caatttgaaa gagatgcaaa cccaccctt 120
 gaatcttacc caggactatg gagctccatt aattgctgtc aacacgctgg aacctatttc 180
 acatgaagct cagaccaatt acaattaatg ccacagtcac gactacaaac tagaaaccaa 240
 tgccagagga agcttaagtt aaagaaagca acgatcacgc acatatatta tgtaggaat 300
 taggcttaat cctagaatcg tgaagccaaa gagaatatat taaagagaga acagtgcctt 360
 cctgggaaga agagcaattt caaatagact ttttagtggc tttctacatt acttacttga 420
 atatattatg ctcccctaga aattactata ttacaattac tcacgccaca ttttatttat 480
 tctcagcaag gaaatgggat ggtgcaatga gctcagtggg cagacggttt ggttatttca 540
 atgaataatt tgaatgtcaa caagttggtg gatgctgatg aaaggggaag tagtaaatag 600
 caaaggctctc aatgcctgac tctgagatgg agtaaggatg agctatcagg actggcactt 660
 cacttctaaa tgttgagcac tcagggtttg ctaaatttat aaaagcacat gaactaacta 720
 acatcgcata tttccttaac gagaaaacca gtttatctct gtttaaaaca gttctgatct 780
 actcaattca ctttttaatt tctgaatgt ttattatcca atttcattac acacgggcgg 840
 caagggagct atctcacacc gaaatacaaa ggtagggat aaccatttct cgccgacaat 900
 tagcaggcca aagaaagtcc tccccgggag cgagggtgga acagatgccc agtgatagga 960
 ccccccaagg ggcccgctgt ccgggtggtc ccca 994

<210> 393
 <211> 802
 <212> DNA
 <213> Homo sapien

<400> 393

433

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ggggagagat ttgaactcag atttgtgcaa ttctaaagcc agcctgttta ttatagtctc      60
ccaggagact acaacagaaa caatgagaaa acaatttgaa agagatgcaa aaccaccccc      120
ttgaatctta cccaggacta tggagctcca ttaattgctg tcaacacgct ggaacctatt      180
tcacatgaag ctacagacaa ttacaattaa tgccacagtc atgactacaa actagaaacc      240
aatgccagag gaagcttaag ttaaagaaag caacgatcac gcacatatat tatgttagca      300
attaggctta atcctagaat cgtgaagcca aagagaatat attaaagaga gaacagtgcc      360
ctcctgggaa gaagagcaat ttcaaataga ctttttagtg gctttctaca ttacttactt      420
gaatatatta tgctccccta gaattactat attacaatta ctcacgccac attttattta      480
tttcagcaag gaaatgggat ggtgcaatga gctcagtggg cagacggttt ggttatttca      540
atgaataatt tgaatgtcaa caagttgggt gatgctgatg aaaggggaag tagtaaatag      600
caaaggctct aatgcctgac tctgagatgg agtaaggatg agctatcagg actggcactt      660
cacttctaaa tggtgagcac tcaggttttg ctaaatttat aaaagcacat gaactaacta      720
acatcgcata tttccttaac gagaaaacca gtttatctct gtttaaaaca gttctgatct      780
actcaaatac acattttaat tt                                     802

```

```

<210> 394
<211> 790
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (454)..(454)
<223> n=a,c,g or t

```

```

<400> 394
catggaacaa taattttaag aacattaatt gttgacatct tggctgccat cacaccaaca      60
gaaatactac catcactcta agccaactct ctcttttacc tttggtttac atgggcatac      120
catatctggc tacagagaaa ttctccagga gtctgcagta cactttcaca ttgtccagca      180
atgctaacat tcaatcttag aggtcattta gcagctcatg actgagttga ttttgtgcag      240
taaggcatag atctataatg aaaaacaaat cttcatttac ttctgttgcc ccatttaatg      300
attatgaaga gtaaactctt ataaagtaaa gtaatactct acttgaaagg aatattcctg      360
ttacactata aaatatatta ccagatatata atttgatggg agaacaaagg aaggatctgt      420
ataaaatata tcaagtaagg ttttacatgt catntataca caactggcag agtttttgag      480
aggctctaata gaaagggtag ttctcatgct ttggaagctc aagtcttct cctcaaagag      540
agtcaatgac agttatttta cagaggatth tgtagaaatg aaaggtaatt aatgccatat      600

```


434

```

aaaagccaaa acattacatc tgtaattgct acatagcatg tgcattgaaa gttgctggtg 660
cccataaggg acagcacttg aaggccaag gaaagagcat acccttcac ctctcagttt 720
gatttgagta ttaaatgagc tagcacacag cttggcacat gttaggcttt cagtatttac 780
cttctttctt 790

```

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<210> 395
<211> 790
<212> DNA
<213> Homo sapien

```

```

<400> 395
catggaacaa taattttaag aacattaatt gttgacatct tggctgccat cacaccaaca 60
gaaatactac catcactcta agccaactct ctcttttacc tttggtttac atgggcatac 120
catatctggc tacagagaaa ttctccagga gtctgcagta cactttcaca ttgtccagca 180
atgctaacat tcaatcttag aggtcattta gcagctcatg actgagttga ttttgtgcag 240
taaggcatag atctataatg aaaaacaaat cttcatttac ttctgttgcc ccatttaatg 300
attatgaaga gtaaactctt ataaagtaaa gtaatactct acttgaaagg aatattcttg 360
ttacactata aaatatatta ccagatatta atttgatggg agaacaaagg aaggatctgc 420
tataaaatat atcaagtaag gttttacatg tcattataca caactgcaga gttttttgag 480
aggctcta at gaaagggtag ttctcatgct ttggaagctc aagtcttcct cctcaaagag 540
agtcaatgac agttatttta cagaggattt tgtagaaatg aaaggtaatt aatgccatat 600
aaaagccaaa acattacatc tgtaattgct acatagcatg tgcattgaaa gttgctggtg 660
cccataaggg acagcacttg aaggccaag gaaagagcat acccttcac ctctcagttt 720
gatttgagta ttaaatgagc tagcacacag cttggcacat gttaggcttt cagtatttac 780
cttctttctt 790

```

```

<210> 396
<211> 690
<212> DNA
<213> Homo sapien

```

```

<400> 396
ggcagtagga aattcaaata ctgagttggg gtgattacac agaactctg tttgaatttt 60
aaaggggaagc aggtatttac ttttggcttt tcttccgtag tttgccttgt gagattaaaa 120
ttgctgatgt ttaaggaaag cagctgttgt ggaaagactt agtgggtttt tatcagagag 180
taaattttga aacaatttgt gggtttttga agtaagggtta cagtatatag tgattagaca 240
gcattttcac tctctcatga aaactgtgta gtcaaaacaa aagtaggaaa aacacatgca 300
taaccctta aatcttattt atgaaaagat aactagcgaa gatgggaaaa tcagacttgt 360

```

435

gtttaagtat catttttttta taaactagct aagtgcattt tgaaacaaaa ttcattgaggt 420
 ctttgtggaa tgccttttcc atttttttgt tttgttttgt tttgtttttg cactcacatt 480
 atgtctcagc aatttaattgg agggctgatt tcctaattgct ttgatccttg gtgagtgtgg 540
 ttcaccccaa ctagggagga attcagtctt ttgttcttga ttccatgctc attgatctcc 600
 tccactgcca ttctcagaaa caatggcagt attttgtttc catagtaatg aaactgtttg 660
 ctctaataagg attctatagt ggtagtgcg 690

<210> 397
 <211> 690
 <212> DNA
 <213> Homo sapien

<400> 397
 ggcagtagga aattcaaata ctgagttggg gtgattacac agaacatctg tttgaatttt 60
 aaaggaagc aggattttac ttttggcttt tcttccgtag tttgccttgt gagattaaaa 120
 ttgctgatgt ttaaggaaag cagctgttgt ggaaagactt agtgggtttt tatcagagag 180
 taaattttga aacaatttgt gggtttttga agtaaggtta cagtatatag tgattagaca 240
 gcattttcac tctctcatga aaactgtgta gtcaaaacaa aagtaggaaa aacacatgca 300
 taaccctta aatcttattt atgaaaagat aactagcgaa gatgggaaaa tcagacttgt 360
 gtttaagtat catttttttta taaactagct aagtgcattt tgaaacaaaa ttcattgaggt 420
 ctttgtggaa tgccttttcc atttttttgt tttgttttgt tttgtttttg cactcacatt 480
 atgtctcagc aatttaattgg agggctgatt tcctaattgct ttgatccttg gtgagtgtgg 540
 ttcaccccaa ctagggagga attcagtctt ttgttcttga ttccatgctc attgatctcc 600
 tccactgcca ttctcagaaa caatggcagt attttgtttc catagtaatg aaactgtttg 660
 ctctaataagg attctatagt ggtaattttt 690

<210> 398
 <211> 879
 <212> DNA
 <213> Homo sapien

<400> 398
 gcctctggga gggaggagcc gagaagcaga ggacagaagc tcccgggcgg gggttaggag 60
 gaaccgagag gactcaggct cccagccttg gggctgatgg agaagaggca attgtcctgc 120
 acgcgcatct ggtggagctc agtggaaattc aactctgctt gctctgcca gagctccacg 180
 tcaatccgct ggtcacttgg aaggaggaag gccctgggag aggggtgcaa agccatacaa 240
 agaaactggt caggcagaac agagaggcag gggctctgag accctgatgg gcagggtggag 300

436

gcttcttcca tgactccgc acttcatgca cccatttggc aaactgtccc atgtgtgcct 360
 gagcaaatgt ggctgttgtg gattctcggt tcataatggc cccaaaaccc aggaacagac 420
 tctgggccac ggcgactcaa gaagtgaaga gtggggctcc cactgtggat gccaggagtc 480
 aaggtgttgc ttgaatatgg gggccacttt gagctggcca tgaacccttc tgtgacaaag 540
 ctcttgggaa agggccattt gggacaccta ggaaggctgg cagcaccaac cagcagcccc 600
 agggagtggg gtgtccaggc caacttgggc acagggtgga gaacagatgc cccagcaggg 660
 ctggcactct tgaaacagaa gcaaggctgt gcacagagtt aatgcccctg acatgcctag 720
 gactgcggta aagtagataa tgcaccttaa gtagccgaca aaactagtga caaaggggtcc 780
 tgaggtcaca atctgaaagg agaaccatt tcactctcgg agatggcaca gaactgggttc 840
 cagctgcaaa ccgggtggag gatacgatag ggagcatcc 879

<210> 399

<211> 879

<212> DNA

<213> Homo sapien

<400> 399

gcctctggga gggaggagcc gagaagcaga ggacagaagc tcccgggagg gggtaggag 60
 gaaccgagag gactcaggct cccagccttg gggctgatgg agaagaggca attgtcctgc 120
 acgcgcactct ggtggagctc agtggaaattc aactctgctt gctctgccc gagctccacg 180
 tcaatccgct ggtcacttgg aaggaggaag gccctgggag aggggtgcaa agccatacaa 240
 agaaactggg caggcagaac agagaggcag gggctctgag accctgatgg gcagggtggag 300
 gcttcttcca tgactccgc acttcatgca cccatttggc aaactgtccc atgtgtgcct 360
 gagcaaatgt ggctgttgtg gattctcggt tcataatggc cccaaaaccc aggaacagac 420
 tctgggccac ggcgactcaa gaagtgaaga gtggggctcc cactgtggat gccaggagtc 480
 aaggtgttgc ttgaatatgg gggccacttt gagctggcca tgaacccttc tgtgacaaag 540
 ctcttgggaa agggccattt gggacaccta ggaaggctgg cagcaccaac cagcagcccc 600
 agggagtggg gtgtccaggc caacttgggc acagggtgga gaacagatgc cccagcaggg 660
 ctggcactct tgaaacagaa gcaaggctgt gcacagagtt aatgcccctg acatgcctag 720
 gactgcggta aagtagataa tgcaccttaa gtagccgaca aaactagtga caaaggggtcc 780
 tgaggtcaca atctgaaagg agaaccatt tcactctcgg agatggcaca gaactgggttc 840
 cagctgcaaa ccgggtggag gatacgatag ggagcatcc 879

<210> 400

<211> 577

<212> DNA

437

<213> Homo sapien

<400> 400

```

agcttgtagg ggaggggtggt gagaaggagg cagccaccca gtgggcgggg atctttcctg      60
gtgactgaga attactgccc cttcacccca gggcctaatt tcccagtc ccacccact      120
atccatccta agactgcagt tgctggccat taccagggat ctggcctctc atccagggtcc      180
ctcctccgct gctccgctgc cacagggcgg ggtctcccag tgccgggcag gcctgcagggt      240
gcggggctgc atggggaggg gggcactcag cagctgctgt acgaggcagg cccctcccc      300
ctcctgctca aagctggagc ctgcttcctg tcgtccctgt cagcacctg ggtgggggag      360
ggaccaggta gtgggggaag tggaaaaggg attgagcggg tggagtgcag cagctgagaa      420
acagcagaag agaaatggag aaggatgacg acaagagacc aagagcatag gctgaaggac      480
cagaggggtg tgagaacaca ggggagatcc caggggctgc agaggctgca gaccctagac      540
tgtgagagcg agaccagagg cagagatgac cagagag      577

```

<210> 401

<211> 574

<212> DNA

<213> Homo sapien

<400> 401

```

agccttgagg ggaggggtggt gagaaggagg cagccaccca gtgggcgggg atctttcctg      60
gtgactgaga attactgccc cttcacccca gggcctaatt tcccagtc ccacccact      120
atccatccta agactgcagt tgctggccat taccagggat ctggcctctc atccagggtcc      180
ctcctccgct gctccgctgc cacagggcgg ggtctcccag tgccgggcag gcctgcagggt      240
gcggggctgc atggggaggg gggcactcag cagctgctgt acgaggcagg cccctcccc      300
ctcctgctca aagctggagc ctgcttcctg tcgtccctgt cagcacctg ggtgggggag      360
ggaccaggta gtgggggaag tggaaaaggg attgagcggg tggagtgcag cagctgagaa      420
acagcagaag agaaatggag aaggatgaga aagagaccaa gagcataggc tgaaggaaag      480
aggggtgtga gaacacaggg gagatcccag gggctgcaga ggctgcagac cctagactgt      540
gagagcgaga ccagaggcag agatgaccag agag      574

```

<210> 402

<211> 3053

<212> DNA

<213> Homo sapien

<400> 402

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agcggggctg gggctccgct ggggaaccgg ccgagcggcg cgcgcggagg tgtccggcgg      60
ccaggaggat ggccaaggct ccgaagctgg aagacacctt cctgcaggcg cagcctgcgc      120

```

438

| | |
|--|------|
| cccaactgtc cccggggatc caggaagact gctgtgtgca gctcctgggc aagggttgc | 180 |
| tagtctatcc ggaagaaaca gtgtacctgg cggccgaagg gcagcccggg ggcgagcagg | 240 |
| gccccgggga gaaaggcgaa gacccggagc tgccgggggc agtgaaatca cgaaatgcac | 300 |
| ttaaacaatg gtaacttttc ctctgaagaa gaggacgccg acaaccacga cagcaaaacc | 360 |
| aaagcagcgg atcaatacct gtctcagaag aaaaccatca cgcagattgt gaaggataaa | 420 |
| aagaagcaga cacagctcac gctgcagtgg cttgaagaga attacattgt atgtgaagga | 480 |
| gtttgcttac cacggtgcat tctttatgca cactacttag atttctgtag gaaagagaaa | 540 |
| ttagagccag cctgtgcggc cacctttgga aagacaattc gccagaagtt tcccctcta | 600 |
| acaacaaggc ggcttggaac aagaggccat tcaaaacaaa tgacatgcac agatgacctg | 660 |
| tttggtcatc tcttaaggta tcattactat gggattggca tcaaagagag cagtgcata | 720 |
| taccactccg tttattctgg aaagggttg acaagggtgg cttcactcgt aaatattcgc | 780 |
| ttagctcaaa aactggaaca cttcttcag aattccccag cgctcaacac cttgtatacc | 840 |
| aaggatgcat ttctaaggac aagcttatta gcagacataa gaaattttgc taaaaattgg | 900 |
| gaacagtggg ttgtttcatc cttggaaaac ttgccagaag ctctaactga caagaaaata | 960 |
| cctattgtgc gaagatttgt atcttctctg aaacgacaaa catctttctt acatcttgcc | 1020 |
| cagattgcc a gaccagctct ctttgaccag catgtcgta attctatggg gtctgatatt | 1080 |
| gaaaggggtg atttgaacag cattggctct caagccctc ttaccatttc aggcagcaca | 1140 |
| gacactgaat ctggtatcta cactgaacgt tcttttcatt tgattogaat gcttctcgat | 1200 |
| gaatacattc tcttgccat ggagaccag tttaataatg acaaagagca ggagttacag | 1260 |
| aatttattgg acaagtatat gaagaattca gatgcgagta aagctgctt cactgcttct | 1320 |
| ccgagttcat gctttctggc caaccgtaat aaaggagca tggtttccag cgacgctgtg | 1380 |
| aagaatgaaa gccacgtgga gacaacctat ctccctctgc catccagtca acctggaggc | 1440 |
| ctaggccctg ctctgcacca gttccctgct gggaacacag acaacatgcc gctcacaggt | 1500 |
| caaattggagc ttacacagat tgctgggtcat ctgatgacac caccatttc tccagccatg | 1560 |
| gcaagccgag gaagtgtcat taaccaagga ccaatggcag ggaggcccc aagtgtgggc | 1620 |
| ccagtactgt cagctccatc aactgctcc acatacccag agccattta tccactctc | 1680 |
| cctcaagcca atcatgactt ttatagcacc agctctaact accagactgt gtttagggca | 1740 |
| cagccccact ccacatcagg actctatcct catcacaccg agcatggctg atgcatggct | 1800 |
| tggactgaac agcagctttc aagagacttc ttcagtggca gctgtgcggg gtctccatat | 1860 |
| aactcccggc caccgtctag ctatggcca tcctgcaag cccaggattc acacaatatg | 1920 |
| cagtttttaa atacaggaag cttcaatttc ttgagcaaca caggagctgc cagctgcca | 1980 |

439

ggagcaacac tgcctcctaa ttcaccaa at ggatactatg gaagcaacat aaactaccca 2040
 gagtctcaca ggctcggatc aatggtgaat cagcacgttt ctgtcatcag cagcattcgt 2100
 tcaactgcccc cctacagtga catccacgat ccacttaaca ttttagatga cagtggtaga 2160
 aaacagacca gctcgtttta cacagacaca tcatctccag ttgcatgtcg aactccagtc 2220
 ctagcttcca gtttgcaaac cccaattcct tcttcctcat cccaatgtat gtatggaact 2280
 tocaaccagt atccagctca agaaaccctg gactcccatg gaacaagcag tagagaaatg 2340
 gtgtcctctt taccacctat caacactgtg ttcattggga cagcagctgg aggcaactaa 2400
 accaccaatg tgggaggggg tgctaaaact ttaaaaaaaaa tctctactgt gcaaatatca 2460
 ttattcactc agacttccat aagagttaa at aaaaatgaat atgcagtggc tgacattgtt 2520
 ttaaagtcac tgggtactatg gacaactcca tagtgaatgg agatacttgc agagcttgtc 2580
 atgcacacta agagttaaaa atgtgagctc attattaatc atagttaaa aattatcaaa 2640
 taaaaccagt gaagatctga agatgcaa ac atttcaacta tgaagattta catttcactt 2700
 tctaatttat taaacatctg tgtgcctttt tatctttggt ttcttttaaa aagtatat 2760
 aatgccttta caataccttt aatttattag gatctcagaa tcattgttta ctatccctta 2820
 tttgacaaaa agtcaa atgt gtatgttcta cctccaacgg aaatgtttac aaggtaaga 2880
 ctttaattcaa ttcagacaag accaaagttg cttgacttca attcctgtgc attagtgtga 2940
 tgattttctgt cacatagcag cattccgatt ctatgtaact gaatggagat gataagtgtc 3000
 ttccctctt tatttaaaaa agattaaaag gaatcaaaga aataatgtat ggc 3053

<210> 403
 <211> 619
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (70)..(167)
 <223> n=a,c,g or t

<400> 403
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 ctgagggagn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 120
 nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnntgt gaatgaagga 180
 gagagtagag caaaataaat aaaaaatcag gggcccatct acatagggtg agatgcttgg 240
 ttcattgtcc aagggtatcg gaagccacta tggcatttga gacgagtga agtttgcatt 300
 actcttcagc aatatcattc tgggtgctct cggaagggtg agtgggtgaa acaaagggtg 360

440

agatcatggg accagtcagg aggctgctgt gttgggtccag gagagaaaag atgggtggttt 420
 gaactacaac cgtgaaagtg cagatggaaa gaggagggtg atgggggata tatttcggcg 480
 gtagcactta agtgaaatgg agttttcttt gtgaaatatg tagaggaaat aatttctggg 540
 agactagcaa gtgggaccaa atggagaaaa aatgattgtc tggtagacca tacagactca 600
 aatttagact aggtatgtg 619

<210> 404
 <211> 918
 <212> DNA
 <213> Homo sapien

<400> 404
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 atagtccagg caaaacatga taaaggcctc aacaagaatg gcaccagtgg agatgaagag 120
 cagaagatca aggtgggaga cagagacaga gaaaacaaag gatttgatgg cttattagat 180
 gtttgggaata ctttaaactt tattcatcct tgctttgctg tgtgcaactg tgtgcatggg 240
 gtgtgcaaca gtggactaga tggcgatgga acctgtgagt gctactctgc gtacactggc 300
 cccaagtgtg acaagcctgg gacagccatg aaagcctcca gtccaaatgc aaaggcaagt 360
 gggtaggaca ggccttctgt ggtcctcagt cagcctcctt ccttggccac tcctgccatt 420
 gtgcagtgga ctctggggca gaggccttct cagtaaggca ggagaccag tccagaagcc 480
 agcctaaggg aaaaccctaa tagatatgct tccaagtaaa aaaataataa taattctgtc 540
 cagccaaatg acaagagact aggacaaaaa tatttaaaat tcacatggca gatacatttt 600
 tataacaaaa aattggattc atgtaaagtc caaaatctaa atttcagaat aagaaatgaa 660
 aacaggcgtg agccacctcg ccacgaggca tcaggcttct ttaaagttag agcacgcctg 720
 tactagagca agcaggaatc agagaccttc cagaaatact actgtgtaag ggccagaaat 780
 atcttcactt gtcattgtta tataatcatt attacttttg ctgtaatgtt aatattgatt 840
 tattaatata tattatcttt tcatacattt tctaagaaac atttatattg ataagatctt 900
 ttattttgcc aagggtt 918

<210> 405
 <211> 3085
 <212> DNA
 <213> Homo sapien

<400> 405
 gcttgccata tgtagaaagc tgaaactgga tcccttcctt acaccttata caaaaattaa 60
 ttcaagatgg attaaagact taaatgtag acctaaaacc ataaaaaact ctagaagaaa 120

441

| | |
|---|------|
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442

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443

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444

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445

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<213> Homo sapien

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447

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Ser Trp Ser Ser Phe Ser Val Pro His Ser Ile Ser Tyr Ser Leu Thr
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Thr Val Pro Val Ile Ser Thr Ser His Ser Arg His Glu Gly Trp Phe
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Pro Cys Lys His Phe Gly Asp Cys Ala Pro Gly Arg
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448

Thr Glu Leu Ile His Gly Tyr Leu Leu Ile Ile Asn Tyr Phe Lys Gln
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His Lys Cys Leu Ser Leu Val Arg Leu Ser Phe Ser Lys His Ser Pro
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 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
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Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

449

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
 210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
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Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
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Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
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Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
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Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg
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Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
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Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
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Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg

450
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 Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu
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 Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys Pro Leu
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 Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu Glu Thr
 645 650 655

451

Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu Lys Met
 660 665 670

Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe Ala Lys
 675 680 685

Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr Ser Ile
 690 695 700

Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn Asn Ile Gly Thr His
 705 710 715 720

Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met Glu Ile
 725 730 735

Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr Asn Leu
 740 745 750

Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile Leu Val Ala Asp Ser
 755 760 765

Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln Met Lys Gly Val Leu
 770 775 780

Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu Ser Pro Ile Leu Pro
 785 790 795 800

Ser Asp Ala Ala Lys Pro Phe Ser Val Val Val Phe His Cys Arg His
 805 810 815

Met Phe His Lys Glu Cys Leu Pro Met Pro Ser Met Asn Ser Ala Ala
 820 825 830

Gln Phe Cys Asn Ile Cys Ser Ala Lys Asn Arg Gly Pro Gly Ser Ala
 835 840 845

Ile Leu Glu Met Lys Lys
 850

<210> 413
 <211> 392
 <212> PRT
 <213> Homo sapien

<400> 413

452

Met Ile Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr
 1 5 10 15
 Leu Ile Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val
 20 25 30
 Gln Ala Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu
 35 40 45
 Leu Lys Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn Tyr Gly Asn
 50 55 60
 Ala Leu Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val Phe Gln Leu
 65 70 75 80
 Ile His Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys Ile Val Leu
 85 90 95
 Leu Met Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu Leu Asp Asn
 100 105 110
 Glu Asp Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu Glu Asp Arg
 115 120 125
 Pro Glu Leu Gln His Val Tyr Leu His Lys Leu Phe Lys Arg Asp His
 130 135 140
 His Lys Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu Tyr Ala Glu
 145 150 155 160
 Tyr Asp Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys
 165 170 175
 Pro Leu Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu
 180 185 190
 Glu Thr Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu
 195 200 205
 Lys Met Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe
 210 215 220
 Ala Lys Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr
 225 230 235 240
 Ser Ile Asp Lys Pro Pro phe Ile Thr Gly Leu Leu Asn Asn Ile Gly

453

245

250

255

Thr His Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met
 260 265 270

Glu Ile Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr
 275 280 285

Asn Leu Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile Leu Val Ala
 290 295 300

Asp Ser Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln Met Lys Gly
 305 310 315 320

Val Leu Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu Ser Pro Ile
 325 330 335

Leu Pro Ser Asp Ala Ala Lys Pro Phe Ser Val Val Val Phe His Cys
 340 345 350

Arg His Met Phe His Lys Glu Cys Leu Pro Met Pro Ser Met Asn Ser
 355 360 365

Ala Ala Gln Phe Cys Asn Ile Cys Ser Ala Lys Asn Arg Gly Pro Gly
 370 375 380

Ser Ala Ile Leu Glu Met Lys Lys
 385 390

<210> 414
 <211> 802
 <212> PRT
 <213> Homo sapien

<400> 414

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

454

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
275 280 285

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
290 295 300

455

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His
 325 330 335

Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg
 340 345 350

Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
 355 360 365

Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
 370 375 380

Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg
 405 410 415

Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu
 420 425 430

Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys Ala Ile Ser Pro Tyr
 435 440 445

Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu Ile Tyr Glu Met Ile
 450 455 460

Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr Leu Ile
 465 470 475 480

Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val Gln Ala
 485 490 495

Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu Leu Lys
 500 505 510

Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn Tyr Gly Asn Ala Leu
 515 520 525

Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val Phe Gln Leu Ile His
 530 535 540

Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys Ile Val Leu Leu Met

456

| | | | | | | |
|---|--|-----|--|-----|--|-----|
| 545 | | 550 | | 555 | | 560 |
| Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu Leu Asp Asn Glu Asp | | | | | | |
| | | 565 | | 570 | | 575 |
| Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu Glu Asp Arg Pro Glu | | | | | | |
| | | 580 | | 585 | | 590 |
| Leu Gln His Val Tyr Leu His Lys Leu Phe Lys Arg Asp His His Lys | | | | | | |
| | | 595 | | 600 | | 605 |
| Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu Tyr Ala Glu Tyr Asp | | | | | | |
| | | 610 | | 615 | | 620 |
| Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys Pro Leu | | | | | | |
| | | 625 | | 630 | | 635 |
| | | | | | | 640 |
| Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu Glu Thr | | | | | | |
| | | 645 | | 650 | | 655 |
| Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu Lys Met | | | | | | |
| | | 660 | | 665 | | 670 |
| Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe Ala Lys | | | | | | |
| | | 675 | | 680 | | 685 |
| Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr Ser Ile | | | | | | |
| | | 690 | | 695 | | 700 |
| Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn Asn Ile Gly Thr His | | | | | | |
| | | 705 | | 710 | | 715 |
| | | | | | | 720 |
| Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met Glu Ile | | | | | | |
| | | 725 | | 730 | | 735 |
| Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr Asn Leu | | | | | | |
| | | 740 | | 745 | | 750 |
| Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile Leu Val Ala Asp Ser | | | | | | |
| | | 755 | | 760 | | 765 |
| Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln Met Lys Gly Val Leu | | | | | | |
| | | 770 | | 775 | | 780 |
| Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu Ser Pro Ile Leu Pro | | | | | | |
| | | 785 | | 790 | | 795 |
| | | | | | | 800 |

457

Ser Glu

<210> 415

<211> 841

<212> PRT

<213> Homo sapien

<400> 415

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

458

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
 210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
 260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
 275 280 285

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
 290 295 300

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His
 325 330 335

Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg
 340 345 350

Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
 355 360 365

Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
 370 375 380

Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg
 405 410 415

Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu
 420 425 430

Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys Ala Ile Ser Pro Tyr

459

435

440

445

Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu Ile Tyr Glu Met Ile
 450 455 460

Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr Leu Ile
 465 470 475 480

Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val Gln Ala
 485 490 495

Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu Leu Lys
 500 505 510

Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn Tyr Gly Asn Ala Leu
 515 520 525

Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val Phe Gln Leu Ile His
 530 535 540

Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys Ile Val Leu Leu Met
 545 550 555 560

Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu Leu Asp Asn Glu Asp
 565 570 575

Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu Glu Asp Arg Pro Glu
 580 585 590

Leu Gln His Val Tyr Leu His Lys Leu Phe Lys Arg Asp His His Lys
 595 600 605

Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu Tyr Ala Glu Tyr Asp
 610 615 620

Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys Pro Leu
 625 630 635 640

Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu Glu Thr
 645 650 655

Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu Lys Met
 660 665 670

Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe Ala Lys
 675 680 685

460

Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr Ser Ile
 690 695 700

Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn Asn Ile Gly Thr His
 705 710 715 720

Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met Glu Ile
 725 730 735

Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr Asn Leu
 740 745 750

Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile Leu Val Ala Asp Ser
 755 760 765

Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln Met Lys Gly Val Leu
 770 775 780

Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu Ser Pro Ile Leu Pro
 785 790 795 800

Ser Asp Ala Ala Lys Pro Phe Ser Val Val Val Phe His Cys Arg His
 805 810 815

Met Phe His Lys Glu Cys Leu Pro Met Pro Ser Met Val Ser Trp Gln
 820 825 830

Leu Gly Thr Tyr Gln Leu Glu Gly Asn
 835 840

<210> 416

<211> 776

<212> PRT

<213> Homo sapien

<400> 416

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

461

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Cys | Met | Thr | Val | His | Asp | Lys | Phe | Leu | Ala | Leu | Gly | Thr | His | Tyr |
| 50 | | | | | | 55 | | | | | 60 | | | | |
| | | | | | | | | | | | | | | | |
| Gly | Lys | Val | Tyr | Leu | Leu | Asp | Val | Gln | Gly | Asn | Ile | Thr | Gln | Lys | Phe |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| | | | | | | | | | | | | | | | |
| Asp | Val | Ser | Pro | Val | Lys | Ile | Asn | Gln | Ile | Ser | Leu | Asp | Glu | Ser | Gly |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| | | | | | | | | | | | | | | | |
| Glu | His | Met | Gly | Val | Cys | Ser | Glu | Asp | Gly | Lys | Val | Gln | Val | Phe | Gly |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| | | | | | | | | | | | | | | | |
| Leu | Tyr | Ser | Gly | Glu | Glu | Phe | His | Glu | Thr | Phe | Asp | Cys | Pro | Ile | Lys |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| | | | | | | | | | | | | | | | |
| Ile | Ile | Ala | Val | His | Pro | His | Phe | Val | Arg | Ser | Ser | Cys | Lys | Gln | Phe |
| | 130 | | | | | 135 | | | | | | 140 | | | |
| | | | | | | | | | | | | | | | |
| Val | Thr | Gly | Gly | Lys | Lys | Leu | Leu | Leu | Phe | Glu | Arg | Ser | Trp | Met | Asn |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| | | | | | | | | | | | | | | | |
| Arg | Trp | Lys | Ser | Ala | Val | Leu | His | Glu | Gly | Glu | Gly | Asn | Ile | Arg | Ser |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| | | | | | | | | | | | | | | | |
| Val | Lys | Trp | Arg | Gly | His | Leu | Ile | Ala | Trp | Ala | Asn | Asn | Met | Gly | Val |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| | | | | | | | | | | | | | | | |
| Lys | Ile | Phe | Asp | Ile | Ile | Ser | Lys | Gln | Arg | Ile | Thr | Asn | Val | Pro | Arg |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| | | | | | | | | | | | | | | | |
| Asp | Asp | Ile | Ser | Leu | Arg | Pro | Asp | Met | Tyr | Pro | Cys | Ser | Leu | Cys | Trp |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| | | | | | | | | | | | | | | | |
| Lys | Asp | Asn | Val | Thr | Leu | Ile | Ile | Gly | Trp | Gly | Thr | Ser | Val | Lys | Val |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| | | | | | | | | | | | | | | | |
| Cys | Ser | Val | Lys | Glu | Arg | His | Ala | Ser | Glu | Met | Arg | Asp | Leu | Pro | Ser |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| | | | | | | | | | | | | | | | |
| Arg | Tyr | Val | Glu | Ile | Val | Ser | Gln | Phe | Glu | Thr | Glu | Phe | Tyr | Ile | Ser |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| | | | | | | | | | | | | | | | |
| Gly | Leu | Ala | Pro | Leu | Cys | Asp | Gln | Leu | Val | Val | Leu | Ser | Tyr | Val | Lys |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| | | | | | | | | | | | | | | | |
| Glu | Ile | Ser | Glu | Lys | Thr | Glu | Arg | Glu | Tyr | Cys | Ala | Arg | Pro | Arg | Leu |

462

| | | |
|---|-----|-------------|
| 290 | 295 | 300 |
| Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp | | |
| 305 | 310 | 315 320 |
| Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His | | |
| | 325 | 330 335 |
| Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg | | |
| | 340 | 345 350 |
| Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp | | |
| | 355 | 360 365 |
| Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile | | |
| | 370 | 375 380 |
| Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala | | |
| | 385 | 390 395 400 |
| Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg | | |
| | 405 | 410 415 |
| Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu | | |
| | 420 | 425 430 |
| Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys Ala Ile Ser Pro Tyr | | |
| | 435 | 440 445 |
| Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu Ile Tyr Glu Met Ile | | |
| | 450 | 455 460 |
| Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr Leu Ile | | |
| | 465 | 470 475 480 |
| Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val Gln Ala | | |
| | 485 | 490 495 |
| Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu Leu Lys | | |
| | 500 | 505 510 |
| Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn Tyr Gly Asn Ala Leu | | |
| | 515 | 520 525 |
| Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val Phe Gln Leu Ile His | | |
| | 530 | 535 540 |

463

Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys Ile Val Leu Leu Met
 545 550 555 560

Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu Leu Asp Asn Glu Asp
 565 570 575

Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu Glu Asp Arg Pro Glu
 580 585 590

Leu Gln His Val Tyr Leu His Lys Leu Phe Lys Arg Asp His His Lys
 595 600 605

Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu Tyr Ala Glu Tyr Asp
 610 615 620

Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys Pro Leu
 625 630 635 640

Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu Glu Thr
 645 650 655

Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu Lys Met
 660 665 670

Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe Ala Lys
 675 680 685

Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr Ser Ile
 690 695 700

Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn Asn Ile Gly Thr His
 705 710 715 720

Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met Glu Ile
 725 730 735

Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr Asn Leu
 740 745 750

Gln Gln Leu Leu Phe Phe Arg Met Leu Val Thr Ser Ile Glu Leu Glu
 755 760 765

Leu Lys His Phe Leu Lys Asn Ser
 770 775

464

<210> 417
 <211> 415
 <212> PRT
 <213> Homo sapien

<400> 417

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp

465

210

215

220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
 260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
 275 280 285

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
 290 295 300

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His
 325 330 335

Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg
 340 345 350

Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
 355 360 365

Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
 370 375 380

Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Asp Ser Glu Val Arg Arg Gly Ser Ser Ile
 405 410 415

<210> 418

<211> 346

<212> PRT

<213> Homo sapien

<400> 418

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

466

Asp Glu Ser Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
 210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

467

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
 260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
 275 280 285

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
 290 295 300

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Cys Asp Leu Gln Glu Phe Pro Ser Ile Arg Pro Pro Val Asp Phe Arg
 325 330 335

Leu Lys His Arg Tyr Ala Met His Ala Leu
 340 345

<210> 419

<211> 158

<212> PRT

<213> Homo sapien

<400> 419

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

468

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Val Ser Ala Val Cys Leu Leu Pro
 145 150 155

<210> 420

<211> 779

<212> PRT

<213> Homo sapien

<400> 420

Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr Gly Lys
 1 5 10 15

Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe Asp Val
 20 25 30

Val Gln Val Phe Gly Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe
 35 40 45

Asp Cys Pro Ile Lys Ile Ile Ala Val His Pro His Phe Val Arg Ser
 50 55 60

Ser Cys Lys Gln Phe Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu
 65 70 75 80

Arg Ser Trp Met Asn Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu
 85 90 95

Gly Asn Ile Arg Ser Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala
 100 105 110

Asn Asn Met Gly Val Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile
 115 120 125

Thr Asn Val Pro Arg Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro
 130 135 140

Cys Ser Leu Cys Trp Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly
 145 150 155 160

Thr Ser Val Lys Val Cys Ser Val Lys Glu Arg His Ala Ser Glu Met
 165 170 175

469

Arg Asp Leu Pro Ser Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr
 180 185 190

Glu Phe Tyr Ile Ser Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val
 195 200 205

Leu Ser Tyr Val Lys Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys
 210 215 220

Ala Arg Pro Arg Leu Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu
 225 230 235 240

Glu Ile Ser Ser Asp Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu
 245 250 255

Cys Arg Asp Tyr His Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr
 260 265 270

Ile Val Ser Pro Arg Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp
 275 280 285

Asp His Ile Asp Trp Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu
 290 295 300

Met Ala Ala Glu Ile Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu
 305 310 315 320

Asp Ile Gly Leu Ala Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr
 325 330 335

Asp Ile Ala Ala Arg Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala
 340 345 350

Leu Trp Glu Tyr Glu Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys
 355 360 365

Ala Ile Ser Pro Tyr Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu
 370 375 380

Ile Tyr Glu Met Ile Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly
 385 390 395 400

Phe Ala Thr Leu Ile Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser
 405 410 415

Val Ile Val Gln Ala Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn

470

420

425

430

Lys Thr Leu Leu Lys Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn
 435 440 445

Tyr Gly Asn Ala Leu Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val
 450 455 460

Phe Gln Leu Ile His Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys
 465 470 475 480

Ile Val Leu Leu Met Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu
 485 490 495

Leu Asp Asn Glu Asp Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu
 500 505 510

Glu Asp Arg Pro Glu Leu Gln His Val Tyr Leu His Lys Leu Phe Lys
 515 520 525

Arg Asp His His Lys Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu
 530 535 540

Tyr Ala Glu Tyr Asp Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser
 545 550 555 560

Thr His Cys Pro Leu Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn
 565 570 575

Phe Val Glu Glu Thr Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg
 580 585 590

Ser Ala Leu Lys Met Ile Met Glu Glu Leu His Asp Val Asp Lys Ala
 595 600 605

Ile Glu Phe Ala Lys Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu
 610 615 620

Ile Leu Tyr Ser Ile Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn
 625 630 635 640

Asn Ile Gly Thr His Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys
 645 650 655

Glu Gly Met Glu Ile Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu
 660 665 670

471

Gln Asp Tyr Asn Leu Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile
 675 680 685

Leu Val Ala Asp Ser Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln
 690 695 700

Met Lys Gly Val Leu Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu
 705 710 715 720

Ser Pro Ile Leu Pro Ser Asp Ala Ala Lys Pro Phe Ser Val Val Val
 725 730 735

Phe His Cys Arg His Met Phe His Lys Glu Cys Leu Pro Met Pro Ser
 740 745 750

Met Asn Ser Ala Ala Gln Phe Cys Asn Ile Cys Ser Ala Lys Asn Arg
 755 760 765

Gly Pro Gly Ser Ala Ile Leu Glu Met Lys Lys
 770 775

<210> 421

<211> 873

<212> PRT

<213> Homo sapien

<400> 421

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

472

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
 210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
 260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
 275 280 285

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
 290 295 300

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His
 325 330 335

Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg

473

340

345

350

Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
 355 360 365

Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
 370 375 380

Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg
 405 410 415

Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu
 420 425 430

Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys Ala Ile Ser Pro Tyr
 435 440 445

Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu Ile Tyr Glu Met Ile
 450 455 460

Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr Leu Ile
 465 470 475 480

Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val Gln Ala
 485 490 495

Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu Leu Lys
 500 505 510

Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn Tyr Gly Asn Ala Leu
 515 520 525

Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val Phe Gln Leu Ile His
 530 535 540

Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys Ile Val Leu Leu Met
 545 550 555 560

Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu Leu Asp Asn Glu Asp
 565 570 575

Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu Glu Asp Arg Pro Glu
 580 585 590

474

Leu Gln His Val Tyr Leu His Lys Leu Phe Lys Arg Asp His His Lys
 595 600 605

Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu Tyr Ala Glu Tyr Asp
 610 615 620

Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys Pro Leu
 625 630 635 640

Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu Glu Thr
 645 650 655

Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu Lys Met
 660 665 670

Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe Ala Lys
 675 680 685

Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr Ser Ile
 690 695 700

Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn Asn Ile Gly Thr His
 705 710 715 720

Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met Glu Ile
 725 730 735

Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr Asn Leu
 740 745 750

Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile Leu Val Ala Asp Ser
 755 760 765

Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln Met Lys Gly Val Leu
 770 775 780

Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu Ser Pro Ile Leu Pro
 785 790 795 800

Ser Asp Ala Ala Lys Pro Phe Ser Val Val Val Phe His Cys Arg His
 805 810 815

Met Phe His Lys Glu Cys Leu Pro Met Pro Ser Met Val Gly Thr Ala
 820 825 830

475

Arg Ile His Leu Tyr Met Asp Phe Leu Leu Pro Leu Pro Pro Leu Arg
 835 840 845

Arg Gln Asp Gln Ala Leu Pro Phe Leu Leu Leu Leu Ser Leu Leu Ser
 850 855 860

Met Lys Thr Thr Glu Met Lys His Leu
 865 870

<210> 422
 <211> 826
 <212> PRT
 <213> Homo sapien

<400> 422

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser

476

165

170

175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
 210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
 260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
 275 280 285

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
 290 295 300

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His
 325 330 335

Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg
 340 345 350

Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
 355 360 365

Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
 370 375 380

Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg
 405 410 415

477

Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu
 420 425 430

Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys Ala Ile Ser Pro Tyr
 435 440 445

Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu Ile Tyr Glu Met Ile
 450 455 460

Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr Leu Ile
 465 470 475 480

Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val Gln Ala
 485 490 495

Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu Leu Lys
 500 505 510

Thr Leu Ala Glu Leu Tyr Thr Tyr Asp Lys Asn Tyr Gly Asn Ala Leu
 515 520 525

Glu Ile Tyr Leu Thr Leu Arg His Lys Asp Val Phe Gln Leu Ile His
 530 535 540

Lys His Asn Leu Phe Ser Ser Ile Lys Asp Lys Ile Val Leu Leu Met
 545 550 555 560

Asp Phe Asp Ser Glu Lys Ala Val Asp Met Leu Leu Asp Asn Glu Asp
 565 570 575

Lys Ile Ser Ile Lys Lys Val Val Glu Glu Leu Glu Asp Arg Pro Glu
 580 585 590

Leu Gln His Val Tyr Leu His Lys Leu Phe Lys Arg Asp His His Lys
 595 600 605

Gly Gln Arg Tyr His Glu Lys Gln Ile Ser Leu Tyr Ala Glu Tyr Asp
 610 615 620

Arg Pro Asn Leu Leu Pro Phe Leu Arg Asp Ser Thr His Cys Pro Leu
 625 630 635 640

Glu Lys Ala Leu Glu Ile Cys Gln Gln Arg Asn Phe Val Glu Glu Thr
 645 650 655

478

Val Tyr Leu Leu Ser Arg Met Gly Asn Ser Arg Ser Ala Leu Lys Met
660 665 670

Ile Met Glu Glu Leu His Asp Val Asp Lys Ala Ile Glu Phe Ala Lys
675 680 685

Glu Gln Asp Asp Gly Glu Leu Trp Glu Asp Leu Ile Leu Tyr Ser Ile
690 695 700

Asp Lys Pro Pro Phe Ile Thr Gly Leu Leu Asn Asn Ile Gly Thr His
705 710 715 720

Val Asp Pro Ile Leu Leu Ile His Arg Ile Lys Glu Gly Met Glu Ile
725 730 735

Pro Asn Leu Arg Asp Ser Leu Val Lys Ile Leu Gln Asp Tyr Asn Leu
740 745 750

Gln Ile Leu Leu Arg Glu Gly Cys Lys Lys Ile Leu Val Ala Asp Ser
755 760 765

Leu Ser Leu Leu Lys Lys Met His Arg Thr Gln Met Lys Gly Val Leu
770 775 780

Val Asp Glu Glu Asn Ile Cys Glu Ser Cys Leu Ser Pro Ile Leu Pro
785 790 795 800

Ser Asp Ala Ala Glu Asn Asn Gly Thr Gly Lys Ser Cys Leu Leu Glu
805 810 815

Lys Lys Leu Ile Pro Thr Ile Ser Leu Ala
820 825

<210> 423

<211> 517

<212> PRT

<213> Homo sapien

<400> 423

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala

479

35

40

45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp
 210 215 220

Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240

Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255

Arg Tyr Val Glu Ile Val Ser Gln Phe Glu Thr Glu Phe Tyr Ile Ser
 260 265 270

Gly Leu Ala Pro Leu Cys Asp Gln Leu Val Val Leu Ser Tyr Val Lys
 275 280 285

480

Glu Ile Ser Glu Lys Thr Glu Arg Glu Tyr Cys Ala Arg Pro Arg Leu
 290 295 300

Asp Ile Ile Gln Pro Leu Ser Glu Thr Cys Glu Glu Ile Ser Ser Asp
 305 310 315 320

Ala Leu Thr Val Arg Gly Phe Gln Glu Asn Glu Cys Arg Asp Tyr His
 325 330 335

Leu Glu Tyr Ser Glu Gly Glu Ser Leu Phe Tyr Ile Val Ser Pro Arg
 340 345 350

Asp Val Val Val Ala Lys Glu Arg Asp Gln Asp Asp His Ile Asp Trp
 355 360 365

Leu Leu Glu Lys Lys Lys Tyr Glu Glu Ala Leu Met Ala Ala Glu Ile
 370 375 380

Ser Gln Lys Asn Ile Lys Arg His Lys Ile Leu Asp Ile Gly Leu Ala
 385 390 395 400

Tyr Ile Asn His Leu Val Glu Arg Gly Asp Tyr Asp Ile Ala Ala Arg
 405 410 415

Lys Cys Gln Lys Ile Leu Gly Lys Asn Ala Ala Leu Trp Glu Tyr Glu
 420 425 430

Val Tyr Lys Phe Lys Glu Ile Gly Gln Leu Lys Ala Ile Ser Pro Tyr
 435 440 445

Leu Pro Arg Gly Asp Pro Val Leu Lys Pro Leu Ile Tyr Glu Met Ile
 450 455 460

Leu His Glu Phe Leu Glu Ser Asp Tyr Glu Gly Phe Ala Thr Leu Ile
 465 470 475 480

Arg Glu Trp Pro Gly Asp Leu Tyr Asn Asn Ser Val Ile Val Gln Ala
 485 490 495

Val Arg Asp His Leu Lys Lys Asp Ser Gln Asn Lys Thr Leu Leu Lys
 500 505 510

Thr Leu Ala Glu Leu
 515

481

<210> 424
 <211> 269
 <212> PRT
 <213> Homo sapien

<400> 424

Met Ala Glu Ala Glu Glu Gln Glu Thr Gly Ser Leu Glu Glu Ser Thr
 1 5 10 15

Asp Glu Ser Glu Glu Glu Glu Ser Glu Glu Glu Pro Lys Leu Lys Tyr
 20 25 30

Glu Arg Leu Ser Asn Gly Val Thr Glu Ile Leu Gln Lys Asp Ala Ala
 35 40 45

Ser Cys Met Thr Val His Asp Lys Phe Leu Ala Leu Gly Thr His Tyr
 50 55 60

Gly Lys Val Tyr Leu Leu Asp Val Gln Gly Asn Ile Thr Gln Lys Phe
 65 70 75 80

Asp Val Ser Pro Val Lys Ile Asn Gln Ile Ser Leu Asp Glu Ser Gly
 85 90 95

Glu His Met Gly Val Cys Ser Glu Asp Gly Lys Val Gln Val Phe Gly
 100 105 110

Leu Tyr Ser Gly Glu Glu Phe His Glu Thr Phe Asp Cys Pro Ile Lys
 115 120 125

Ile Ile Ala Val His Pro His Phe Val Arg Ser Ser Cys Lys Gln Phe
 130 135 140

Val Thr Gly Gly Lys Lys Leu Leu Leu Phe Glu Arg Ser Trp Met Asn
 145 150 155 160

Arg Trp Lys Ser Ala Val Leu His Glu Gly Glu Gly Asn Ile Arg Ser
 165 170 175

Val Lys Trp Arg Gly His Leu Ile Ala Trp Ala Asn Asn Met Gly Val
 180 185 190

Lys Ile Phe Asp Ile Ile Ser Lys Gln Arg Ile Thr Asn Val Pro Arg
 195 200 205

Asp Asp Ile Ser Leu Arg Pro Asp Met Tyr Pro Cys Ser Leu Cys Trp

482

210 215 220
 Lys Asp Asn Val Thr Leu Ile Ile Gly Trp Gly Thr Ser Val Lys Val
 225 230 235 240
 Cys Ser Val Lys Glu Arg His Ala Ser Glu Met Arg Asp Leu Pro Ser
 245 250 255
 Arg Tyr Val Glu Ile Val Ser Ala Asp Pro Val Val Lys
 260 265
 <210> 425
 <211> 60
 <212> PRT
 <213> Homo sapien
 <400> 425
 Met Lys Asn Glu Asn Lys Ala Gln Arg Ser Lys Lys Thr Cys Leu Gln
 1 5 10 15
 Glu Ser Ala Ser Glu Asp Gln Gln Glu Thr Glu Asn Leu Gln Asn Ser
 20 25 30
 Leu Leu Ile Gln Lys Ile Ile Gln Asn Ser Thr Met Pro Gln Ser Asp
 35 40 45
 Gln Tyr Lys Phe Glu Val Leu Leu Lys Thr Lys Ala
 50 55 60
 <210> 426
 <211> 96
 <212> PRT
 <213> Homo sapien
 <400> 426
 Met Thr His Tyr Arg Glu Lys His Val Ser Gln Glu Cys Ile Gln Ile
 1 5 10 15
 Asp Thr Leu Lys Lys His Thr Gly Ile Leu Ala Trp Gly Arg Gly Arg
 20 25 30
 Thr Leu Gly Ile Thr Cys Lys Ile Ile Ser Glu Ser Lys Ile Glu Asn
 35 40 45
 His Leu Leu Ser His Lys Ala Lys Cys His Ser Val Arg Glu Met Trp
 50 55 60

483

Thr Glu Gln Arg Arg Leu Ala Gly Arg Cys Ser Gln Ala Pro Ser Ile
 65 70 75 80

Asn His Thr Gln Cys Cys Leu His Leu Val Pro Gly Ser Gln Arg Leu
 85 90 95

<210> 427
 <211> 56
 <212> PRT
 <213> Homo sapien

<400> 427

Phe Trp Val Ala Gln Leu Leu Val Asn Gly Leu Ser Cys Glu Arg Gly
 1 5 10 15

Pro Arg Val Asp Val Gln Gln Leu Ala Pro Pro Pro Pro Gln Gln
 20 25 30

Pro Pro Gln Ala Pro Gln Ala Ala Gly Ala Ala Ala Thr Pro Ala Leu
 35 40 45

Leu Phe Ile Phe Leu Ser Leu His
 50 55

<210> 428
 <211> 317
 <212> PRT
 <213> Homo sapien

<400> 428

Met Ala Ala Ala Ala Gly Ser Cys Ala Arg Val Ala Ala Trp Gly Gly
 1 5 10 15

Lys Leu Arg Arg Gly Leu Ala Val Ser Arg Gln Ala Val Arg Ser Pro
 20 25 30

Gly Pro Leu Ala Ala Ala Val Ala Gly Ala Ala Leu Ala Gly Ala Gly
 35 40 45

Ala Ala Trp His His Ser Arg Val Ser Val Ala Ala Arg Asp Gly Ser
 50 55 60

Phe Thr Val Ser Ala Gln Lys Asn Val Glu His Gly Ile Ile Tyr Ile
 65 70 75 80

Gly Lys Pro Ser Leu Arg Lys Gln Arg Phe Met Gln Phe Ser Ser Leu
 85 90 95

484

Glu His Glu Gly Glu Tyr Tyr Met Thr Pro Arg Asp Phe Leu Phe Ser
 100 105 110

Val Met Phe Glu Gln Met Glu Arg Lys Thr Ser Val Lys Lys Leu Thr
 115 120 125

Lys Lys Asp Ile Glu Asp Thr Leu Ser Gly Ile Gln Thr Ala Gly Cys
 130 135 140

Gly Ser Thr Phe Phe Arg Asp Leu Gly Asp Lys Gly Leu Ile Ser Tyr
 145 150 155 160

Thr Glu Tyr Leu Phe Leu Leu Thr Ile Leu Thr Lys Pro His Ser Gly
 165 170 175

Phe His Val Ala Phe Lys Met Leu Asp Thr Asp Gly Asn Glu Met Ile
 180 185 190

Glu Lys Arg Glu Phe Phe Lys Leu Gln Lys Ile Ile Ser Lys Gln Asp
 195 200 205

Asp Leu Met Thr Val Lys Thr Asn Glu Thr Gly Tyr Gln Glu Ala Ile
 210 215 220

Val Lys Glu Pro Glu Ile Asn Thr Thr Leu Gln Met Arg Phe Phe Gly
 225 230 235 240

Lys Arg Gly Gln Arg Lys Leu His Tyr Lys Glu Phe Arg Arg Phe Met
 245 250 255

Glu Asn Leu Gln Thr Glu Ile Gln Glu Met Glu Phe Leu Gln Phe Ser
 260 265 270

Lys Gly Leu Ser Phe Met Arg Lys Glu Asp Phe Ala Glu Trp Leu Leu
 275 280 285

Phe Phe Thr Asn Thr Glu Asn Lys Asp Ile Tyr Trp Lys Asn Val Arg
 290 295 300

Glu Lys Leu Ser Ala Gly Glu Arg Ser Leu Arg Glu Leu
 305 310 315

<210> 429

<211> 425

<212> PRT

<213> Homo sapien

485

<400> 429

Met Ala Ala Ala Ala Gly Ser Cys Ala Arg Val Ala Ala Trp Gly Gly
 1 5 10 15

Lys Leu Arg Arg Gly Leu Ala Val Ser Arg Gln Ala Val Arg Ser Pro
 20 25 30

Gly Pro Leu Ala Ala Ala Val Ala Gly Ala Ala Leu Ala Gly Ala Gly
 35 40 45

Ala Ala Trp His His Ser Arg Val Ser Val Ala Ala Arg Asp Gly Ser
 50 55 60

Phe Thr Val Ser Ala Gln Lys Asn Val Glu His Gly Ile Ile Tyr Ile
 65 70 75 80

Gly Lys Pro Ser Leu Arg Lys Gln Arg Phe Met Gln Phe Ser Ser Leu
 85 90 95

Glu His Glu Gly Glu Tyr Tyr Met Thr Pro Arg Asp Phe Leu Phe Ser
 100 105 110

Val Met Phe Glu Gln Met Glu Arg Lys Thr Ser Val Lys Lys Leu Thr
 115 120 125

Lys Lys Asp Ile Glu Asp Thr Leu Ser Gly Ile Gln Thr Ala Gly Cys
 130 135 140

Gly Ser Thr Phe Phe Arg Asp Leu Gly Asp Lys Gly Leu Ile Ser Tyr
 145 150 155 160

Thr Glu Tyr Leu Phe Leu Leu Thr Ile Leu Thr Lys Pro His Ser Gly
 165 170 175

Phe His Val Ala Phe Lys Met Leu Asp Thr Asp Gly Asn Glu Met Ile
 180 185 190

Glu Lys Arg Glu Phe Phe Lys Leu Gln Lys Ile Ile Ser Lys Gln Asp
 195 200 205

Asp Leu Met Thr Val Lys Thr Asn Glu Thr Gly Tyr Gln Glu Ala Ile
 210 215 220

Val Lys Glu Pro Glu Ile Asn Thr Thr Leu Gln Met Arg Phe Phe Gly
 225 230 235 240

Lys Arg Gly Gln Arg Lys Leu His Tyr Lys Glu Phe Arg Arg Phe Met
245 250 255

Lys Gly Leu Ser Phe Met Arg Lys Glu Asp Phe Ala Glu Trp Leu Leu
275 280 285

Phe Phe Thr Asn Thr Glu Asn Lys Asp Ile Tyr Trp Lys Asn Val Arg
290 295 300

Glu Lys Leu Ser Ala Gly Glu Ser Ile Ser Leu Asp Glu Phe Lys Ser
305 310 315 320

Phe Cys His Phe Thr Thr His Leu Glu Asp Phe Ala Ile Ala Met Gln
325 330 335

Met Phe Ser Leu Ala His Arg Pro Val Arg Leu Ala Glu Phe Lys Arg
340 345 350

Ala Val Lys Val Ala Thr Gly Gln Glu Leu Ser Asn Asn Ile Leu Asp
355 360 365

Thr Val Phe Lys Ile Phe Asp Leu Asp Gly Asp Glu Cys Leu Ser His
370 375 380

Glu Glu Phe Leu Gly Val Leu Lys Asn Arg Met His Arg Gly Leu Trp
385 390 395 400

Ser Pro Thr Phe Gln Gly Ser Glu Asn Trp Lys Gly Trp Arg Lys Glu
405 410 415

Pro Leu Arg Arg Glu Gly Gly Asn Leu
420 425

| | |
|-------|-------------|
| <210> | 430 |
| <211> | 327 |
| <212> | PRT |
| <213> | Homo sapien |

<400> 430

Met Ala Ala Ala Ala Gly Ser Cys Ala Arg Val Ala Ala Trp Gly Gly
1 5 10 15

487

Lys Leu Arg Arg Gly Leu Ala Val Ser Arg Gln Ala Val Arg Ser Pro
 20 25 30

Gly Pro Leu Ala Ala Ala Val Ala Gly Ala Ala Leu Ala Gly Ala Gly
 35 40 45

Ala Ala Trp His His Ser Arg Val Ser Val Ala Ala Arg Asp Gly Ser
 50 55 60

Phe Thr Val Ser Ala Gln Lys Asn Val Glu His Gly Ile Ile Tyr Ile
 65 70 75 80

Gly Lys Pro Ser Leu Arg Lys Gln Arg Phe Met Gln Phe Ser Ser Leu
 85 90 95

Glu His Glu Gly Glu Tyr Tyr Met Thr Pro Arg Asp Phe Leu Phe Ser
 100 105 110

Val Met Phe Glu Gln Met Glu Arg Lys Thr Ser Val Lys Lys Leu Thr
 115 120 125

Lys Lys Asp Ile Glu Asp Thr Leu Ser Gly Ile Gln Thr Ala Gly Cys
 130 135 140

Gly Ser Thr Phe Phe Arg Asp Leu Gly Asp Lys Gly Leu Ile Ser Tyr
 145 150 155 160

Thr Glu Tyr Leu Phe Leu Leu Thr Ile Leu Thr Lys Pro His Ser Gly
 165 170 175

Phe His Val Ala Phe Lys Met Leu Asp Thr Asp Gly Asn Glu Met Ile
 180 185 190

Glu Lys Arg Glu Phe Phe Lys Leu Gln Lys Ile Ile Ser Lys Gln Asp
 195 200 205

Asp Leu Met Thr Val Lys Thr Asn Glu Thr Gly Tyr Gln Glu Ala Ile
 210 215 220

Val Lys Glu Pro Glu Ile Asn Thr Thr Leu Gln Met Arg Phe Phe Gly
 225 230 235 240

Lys Arg Gly Gln Arg Lys Leu His Tyr Lys Glu Phe Arg Arg Phe Met
 245 250 255

Glu Asn Leu Gln Thr Glu Ile Gln Glu Met Glu Phe Leu Gln Phe Ser

488

260

265

270

Lys Gly Leu Ser Phe Met Arg Lys Glu Asp Phe Ala Glu Trp Leu Leu
 275 280 285

Phe Phe Thr Asn Thr Glu Asn Lys Asp Ile Tyr Trp Lys Asn Val Arg
 290 295 300

Glu Lys Leu Ser Ala Gly Glu Val Gly Ile Pro Phe Tyr Tyr Ala Cys
 305 310 315 320

Asp Lys Asp Glu Ile Ile Ser
 325

<210> 431
 <211> 203
 <212> PRT
 <213> Homo sapien

<400> 431

Met Ala Ala Ala Ala Gly Ser Cys Ala Arg Val Ala Ala Trp Gly Gly
 1 5 10 15

Lys Leu Arg Arg Gly Leu Ala Val Ser Arg Gln Ala Val Arg Ser Pro
 20 25 30

Gly Pro Leu Ala Ala Ala Val Ala Gly Ala Ala Leu Ala Gly Ala Gly
 35 40 45

Ala Ala Trp His His Ser Arg Val Ser Val Ala Ala Arg Asp Gly Ser
 50 55 60

Phe Thr Val Ser Ala Gln Lys Asn Val Glu His Gly Ile Ile Tyr Ile
 65 70 75 80

Gly Lys Pro Ser Leu Arg Lys Gln Arg Phe Met Gln Phe Ser Ser Leu
 85 90 95

Glu His Glu Gly Glu Tyr Tyr Met Thr Pro Arg Asp Phe Leu Phe Ser
 100 105 110

Val Met Phe Glu Gln Met Glu Arg Lys Thr Ser Val Lys Lys Leu Thr
 115 120 125

Lys Lys Asp Ile Glu Asp Thr Leu Ser Gly Ile Gln Thr Ala Gly Cys
 130 135 140

489

Gly Ser Thr Phe Phe Arg Asp Leu Gly Asp Lys Gly Leu Ile Ser Tyr
 145 150 155 160

Thr Glu Tyr Leu Phe Leu Leu Thr Ile Leu Thr Lys Pro His Ser Gly
 165 170 175

Phe His Val Ala Phe Lys Met Leu Asp Thr Asp Gly Asn Glu Met Ile
 180 185 190

Glu Lys Arg Glu Phe Phe Lys Val Ser Gly Arg
 195 200

<210> 432
 <211> 176
 <212> PRT
 <213> Homo sapien

<220>
 <221> MISC_FEATURE
 <222> (36)..(36)
 <223> x= any amino acid

<220>
 <221> MISC_FEATURE
 <222> (53)..(53)
 <223> x= any amino acid

<220>
 <221> MISC_FEATURE
 <222> (58)..(58)
 <223> x= any amino acid

<400> 432

Arg Thr Ala Gln Gln Gln Gln Lys Ser Asn Lys Thr Leu Val Gly Pro
 1 5 10 15

Cys Gly Ala Leu Lys Ser Ser Ser Phe Phe Thr Ala Ser Ser Leu Ser
 20 25 30

Val Asn Arg Xaa Arg Ile Ser Glu Asp Ser Phe Val Ile His Asn Gly
 35 40 45

Gln Leu Val Asp Xaa Ile Ser Val Gly Xaa Lys Pro Phe Tyr Asp Arg
 50 55 60

Met Ser Met Cys Trp Asp Ser Pro Ser Phe Gln Asp Gln Ile Lys Thr
 65 70 75 80

490

Asp Val Arg Ala Ile Ile Gln Val Glu Val Tyr Leu Val Leu Lys Tyr
85 90 95

Trp Leu Pro Phe Pro Gly Gly Met Ile Pro Cys Ser Thr Asn Ser Asn
100 105 110

Asn Gly Ser Ser Ser Ser Leu Thr Ser Val Asn Leu Thr Phe Arg Ser
115 120 125

Ser Ile Ser Ser Lys Ser Ser Gly Asp Ser Phe Arg Asn Ile Phe Ser
130 135 140

Phe Ser Phe Thr Glu Thr Leu Ala Lys Ser Phe Ile Asp Pro Cys Leu
145 150 155 160

Ser Leu Ile Tyr Leu Arg His Cys Ser Cys Arg Ile Arg His Glu Gly
165 170 175

<210> 433

<211> 443

<212> PRT

<213> Homo sapien

<400> 433

Met Ala Ala Ala Ala Gly Ser Cys Ala Arg Val Ala Ala Trp Gly Gly
1 5 10 15

Lys Leu Arg Arg Gly Leu Ala Val Ser Arg Gln Ala Val Arg Ser Pro
20 25 30

Gly Pro Leu Ala Ala Ala Val Ala Gly Ala Ala Leu Ala Gly Ala Gly
35 40 45

Ala Ala Trp His His Ser Arg Val Ser Val Ala Ala Arg Asp Gly Ser
50 55 60

Phe Thr Val Ser Ala Gln Lys Asn Val Glu His Gly Ile Ile Tyr Ile
65 70 75 80

Gly Lys Pro Ser Leu Arg Lys Gln Arg Phe Met Gln Phe Ser Ser Leu
85 90 95

Glu His Glu Gly Glu Tyr Tyr Met Thr Pro Arg Asp Phe Leu Phe Ser
100 105 110

Val Met Phe Glu Gln Met Glu Arg Lys Thr Ser Val Lys Lys Leu Thr

491

115

120

125

Lys Lys Asp Ile Glu Asp Thr Leu Ser Gly Ile Gln Thr Ala Gly Cys
 130 135 140

Gly Ser Thr Phe Phe Arg Asp Leu Gly Asp Lys Gly Leu Ile Ser Tyr
 145 150 155 160

Thr Glu Tyr Leu Phe Leu Leu Thr Ile Leu Thr Lys Pro His Ser Gly
 165 170 175

Phe His Val Ala Phe Lys Met Leu Asp Thr Asp Gly Asn Glu Met Ile
 180 185 190

Glu Lys Arg Glu Phe Phe Lys Asp Asp Thr Ile Asp Ser Glu Arg Gln
 195 200 205

Leu Gln Lys Ile Ile Ser Lys Gln Asp Asp Leu Met Thr Val Lys Thr
 210 215 220

Asn Glu Thr Gly Tyr Gln Glu Ala Ile Val Lys Glu Pro Glu Ile Asn
 225 230 235 240

Thr Thr Leu Gln Met Arg Phe Phe Gly Lys Arg Gly Gln Arg Lys Leu
 245 250 255

His Tyr Lys Glu Phe Arg Arg Phe Met Glu Asn Leu Gln Thr Glu Ile
 260 265 270

Gln Glu Met Glu Phe Leu Gln Phe Ser Lys Gly Leu Ser Phe Met Arg
 275 280 285

Lys Glu Asp Phe Ala Glu Trp Leu Leu Phe Phe Thr Asn Thr Glu Asn
 290 295 300

Lys Asp Ile Tyr Trp Lys Asn Val Arg Glu Lys Leu Ser Ala Gly Glu
 305 310 315 320

.Ser Ile Ser Leu Asp Glu Phe Lys Ser Phe Cys His Phe Thr Thr His
 325 330 335

Leu Glu Asp Phe Ala Ile Ala Met Gln Met Phe Ser Leu Ala His Arg
 340 345 350

Pro Val Arg Leu Ala Glu Phe Lys Arg Ala Val Lys Val Ala Thr Gly
 355 360 365

492

Gln Glu Leu Ser Asn Asn Ile Leu Asp Thr Val Phe Lys Ile Phe Asp
 370 375 380

Leu Asp Gly Asp Glu Cys Leu Ser His Glu Glu Phe Leu Gly Val Leu
 385 390 395 400

Lys Asn Arg Met His Arg Gly Leu Trp Val Pro Gln His Gln Ser Ile
 405 410 415

Gln Glu Tyr Trp Lys Cys Val Lys Lys Glu Ser Ile Lys Gly Val Lys
 420 425 430

Glu Val Trp Lys Gln Ala Gly Lys Gly Leu Phe
 435 440

<210> 434

<211> 382

<212> PRT

<213> Homo sapien

<400> 434

Met Ala Ala Ala Ala Gly Ser Cys Ala Arg Val Ala Ala Trp Gly Gly
 1 5 10 15

Lys Leu Arg Arg Gly Leu Ala Val Ser Arg Gln Ala Val Arg Ser Pro
 20 25 30

Gly Pro Leu Ala Ala Ala Val Ala Gly Ala Ala Leu Ala Gly Ala Gly
 35 40 45

Ala Ala Trp His His Ser Arg Val Ser Val Ala Ala Arg Asp Gly Ser
 50 55 60

Phe Thr Val Ser Ala Gln Lys Asn Val Glu His Gly Ile Ile Tyr Ile
 65 70 75 80

Gly Lys Pro Ser Leu Arg Lys Gln Arg Phe Met Gln Phe Ser Ser Leu
 85 90 95

Glu His Glu Gly Glu Tyr Tyr Met Thr Pro Arg Asp Phe Leu Phe Ser
 100 105 110

Val Met Phe Glu Gln Met Glu Arg Lys Thr Ser Val Lys Lys Leu Thr
 115 120 125

493

Lys Lys Asp Ile Glu Asp Thr Leu Ser Gly Ile Gln Thr Ala Gly Cys
 130 135 140

Gly Ser Thr Phe Phe Arg Asp Leu Gly Asp Lys Gly Leu Ile Ser Tyr
 145 150 155 160

Thr Glu Tyr Leu Phe Leu Leu Thr Ile Leu Thr Lys Pro His Ser Gly
 165 170 175

Phe His Val Ala Phe Lys Met Leu Asp Thr Asp Gly Asn Glu Met Ile
 180 185 190

Glu Lys Arg Glu Phe Phe Lys Leu Gln Lys Ile Ile Ser Lys Gln Asp
 195 200 205

Asp Leu Met Thr Val Lys Thr Asn Glu Thr Gly Tyr Gln Glu Ala Ile
 210 215 220

Val Lys Glu Pro Glu Ile Asn Thr Thr Leu Gln Met Arg Phe Phe Gly
 225 230 235 240

Lys Arg Gly Gln Arg Lys Leu His Tyr Lys Glu Phe Arg Arg Phe Met
 245 250 255

Glu Asn Leu Gln Thr Glu Ile Gln Glu Met Glu Phe Leu Gln Phe Ser
 260 265 270

Lys Gly Leu Ser Phe Met Arg Lys Glu Asp Phe Ala Glu Trp Leu Leu
 275 280 285

Phe Phe Thr Asn Thr Glu Asn Lys Asp Ile Tyr Trp Lys Asn Val Arg
 290 295 300

Glu Lys Leu Ser Ala Gly Glu Ser Ile Ser Leu Asp Glu Phe Lys Ser
 305 310 315 320

Phe Cys His Phe Thr Thr His Leu Glu Asp Phe Ala Ile Ala Ile Ala
 325 330 335

Lys Val Gln Leu Thr Tyr Met Ala Gly Arg Gln Arg Gly Val Lys Glu
 340 345 350

Arg Trp Lys Gly His Thr Gly Arg Asp Leu Asn Asn Asn Leu Gly Asn
 355 360 365

Gly Leu Lys Thr Leu Phe Gly Leu Glu Glu Ser Ala Lys Gln

494

370

375

380

<210> 435
 <211> 53
 <212> PRT
 <213> Homo sapien

<400> 435

Met Lys Pro Pro Ser Leu Leu Thr Cys His Asn Tyr Gln Gly Tyr Leu
 1 5 10 15

Gln Lys Lys Val Lys Ala Lys Thr Ser Glu Val Glu Gly Ile Ile His
 20 25 30

Phe Cys Ile Leu Ser Ser Gly Lys Ala Ile Glu Phe Lys Phe Asn Asn
 35 40 45

Asn Asn Asn Asp Asp
 50

<210> 436
 <211> 59
 <212> PRT
 <213> Homo sapien

<400> 436

Met Pro Phe Val Ile Val Thr Ile Ile Asn Ala Ile Thr Asp Phe His
 1 5 10 15

Asp Ser Pro Ser Cys Pro Ile Tyr Cys Gln Ile Pro His Leu Pro Ile
 20 25 30

Pro Glu Ala Met Leu Gly Gly Gln Gln Gln Thr Gln Asp Asn Leu Glu
 35 40 45

Ser Trp Gly Val His His Ile Asp Glu His Val
 50 55

<210> 437
 <211> 24
 <212> PRT
 <213> Homo sapien

<400> 437

Met Phe Gly Asp Gln Asn Lys Val Leu Phe Cys Met Asn Ser Cys Gln
 1 5 10 15

Gly Ile Glu Leu Lys His Glu Lys

495

20

<210> 438
 <211> 45
 <212> PRT
 <213> Homo sapien

<400> 438

Met Pro Ala Asn Ser Thr Pro Ser Leu His Asn Phe Ser Val Leu Leu
 1 5 10 15

Ser Leu His Phe Ile Tyr Cys Leu Glu Leu Phe Ala Asn Leu Tyr Lys
 20 25 30

Leu Ile Phe Pro Tyr Pro Ser Ala Leu Tyr Thr Val Gly
 35 40 45

<210> 439
 <211> 112
 <212> PRT
 <213> Homo sapien

<400> 439

Met Ser Glu Ala Ser Arg Leu Cys Ser Gly Tyr Tyr Ser Leu Asn Gln
 1 5 10 15

Ser Phe Val Glu Pro Phe Gln Cys Pro Arg Arg Gly Glu Gly Ala Ala
 20 25 30

Leu Gln Tyr Cys Cys Gly Phe Ala Asp Leu Lys Tyr Cys Cys Ser Glu
 35 40 45

Pro Gly Ser Tyr Phe Pro Tyr Lys His Ser Tyr Met Trp Ser Leu Arg
 50 55 60

Trp Ala Glu Ser Pro Arg Val Arg Arg Leu Ala Glu Pro Gly Ala Arg
 65 70 75 80

Glu Ala Thr Ser Gly Ala Thr Pro Gly Pro Gly Arg Phe Pro Arg Val
 85 90 95

Pro Ala Ile Arg Pro Arg Leu Gly Pro Tyr Gly Arg Thr Arg Ser Leu
 100 105 110

<210> 440
 <211> 15
 <212> PRT
 <213> Homo sapien

496

<400> 440

Met Leu Leu Lys Lys Asn Tyr Asn Leu Thr Ala Cys Leu Arg Arg
1 5 10 15

<210> 441

<211> 29

<212> PRT

<213> Homo sapien

<400> 441

Met Lys Ser Thr Ser Arg His Ala Ile Lys Lys Ser Tyr Asp Gln Pro
1 5 10 15

Glu Lys Lys Tyr Arg Ser Ser Ser Asn Glu Gln Gln Leu
20 25

<210> 442

<211> 41

<212> PRT

<213> Homo sapien

<400> 442

Met Thr Asn Pro Gly Ser Asn Thr Tyr Gln Ser Gly Lys Ile Arg Thr
1 5 10 15

Gln Asn Lys Glu Lys Leu Gly Pro Cys Thr Ile Ser Ala Thr Ile Lys
20 25 30

Tyr Glu Tyr Thr Ser Glu Leu Ser Gly
35 40

<210> 443

<211> 28

<212> PRT

<213> Homo sapien

<400> 443

Met Val Thr Glu Ile Phe Gln Asn Ser Thr Leu His Asn Phe Asn Val
1 5 10 15

Ser Thr His Glu His Lys His Leu Met Val Asn Leu
20 25

<210> 444

<211> 121

<212> PRT

<213> Homo sapien

497

<400> 444

Met Lys Ile Ala Thr Lys Lys Arg Asn Ser Val His Val Thr Phe Arg
 1 5 10 15

Pro Ser Thr Glu Ser Val Gln Phe Tyr Asn Pro Leu Glu Asn Lys Glu
 20 25 30

Ala Pro Trp Lys Met Arg Leu Arg Lys Leu Gly Gly Phe Ser Ser Gly
 35 40 45

Ser Ser Asn Ser Ser Thr Ser Asn Thr His Thr Ser Thr Asn Ser Ala
 50 55 60

Thr Glu Leu Val Lys Pro Gly Val Tyr Arg Pro Leu Asp Thr Leu Gly
 65 70 75 80

Thr Ala Ser Val Ser Ser Lys Thr Val Lys Glu Ser Thr Glu Ile Pro
 85 90 95

Thr Thr Ile Leu Gln Lys Glu Gly Ile Ala Ser Ser Gln Leu Gly Ser
 100 105 110

Arg Ser Thr Leu Arg Ser Ser Ser His
 115 120

<210> 445

<211> 955

<212> PRT

<213> Homo sapien

<400> 445

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

| | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Glu | Asn | Gln | Glu | Arg | Gly | Phe | Ser | Phe | Leu | Phe | Ser | His | Phe | Lys | 85 | 90 | 95 |
| Lys | Tyr | Tyr | Leu | Pro | Tyr | Ile | Phe | Pro | Asn | Ile | Cys | Lys | Glu | Asn | Ser | 100 | 105 | 110 |
| Leu | Tyr | His | Pro | Ile | Leu | Asp | Ile | Pro | Gln | Met | Arg | Pro | Lys | Pro | His | 115 | 120 | 125 |
| Tyr | Val | Val | Ile | Lys | Lys | Asp | Ala | Glu | Thr | Asn | Glu | Ala | Ile | Tyr | Cys | 130 | 135 | 140 |
| Thr | Lys | Glu | Pro | Phe | Ile | Lys | Ala | Arg | Val | Ile | Val | Ile | Arg | Trp | Leu | 145 | 150 | 155 |
| Val | Ser | Phe | Trp | Leu | Glu | Pro | Lys | Pro | His | Thr | Gly | Pro | His | Ile | Pro | 165 | 170 | 175 |
| Gly | Met | Glu | Gly | Glu | Val | Leu | Pro | Lys | Asn | Ile | Gln | Arg | Ala | Ala | Ala | 180 | 185 | 190 |
| Ser | Leu | Val | Ser | Arg | Glu | Glu | Ser | Lys | Asn | Asp | Asn | Ala | Asp | Lys | Thr | 195 | 200 | 205 |
| Asp | Arg | Thr | Thr | Glu | Pro | Glu | Gln | Ser | His | Ser | Asn | Thr | Ser | Thr | Leu | 210 | 215 | 220 |
| Thr | Glu | Arg | Glu | Pro | Ser | Ser | Ser | Ser | Leu | Cys | Ser | Ile | Asp | Glu | Glu | 225 | 230 | 235 |
| His | Leu | Thr | Asp | Ile | Glu | Ile | Val | Arg | Arg | Val | Phe | Ser | Ser | Lys | Arg | 245 | 250 | 255 |
| Ser | Asn | Val | Asn | Phe | Val | Thr | Glu | Ile | Phe | Arg | Gln | Ala | Phe | Leu | Leu | 260 | 265 | 270 |
| Pro | Ile | Cys | Glu | Ala | Ala | Ala | Met | Arg | Lys | Val | Val | Lys | Val | Tyr | Gln | 275 | 280 | 285 |
| Glu | Trp | Ile | Gln | Gln | Glu | Glu | Lys | Pro | Leu | Phe | Met | Gln | Glu | Pro | Glu | 290 | 295 | 300 |
| Glu | Ile | Val | Ile | Thr | Ser | Ser | Asp | Leu | Pro | Cys | Ile | Glu | Asn | Val | Thr | 305 | 310 | 315 |
| Asp | His | Asp | Ile | Ser | Met | Glu | Glu | Gly | Glu | Lys | Arg | Glu | Glu | Glu | Asn | 320 | | |

499

325

330

335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

500

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Ala Met
 595 600 605

Arg Ser Arg Ser Ile Gly Glu Cys Ala Leu Pro Ser Ala Tyr Ile Arg
 610 615 620

Ser Ala Lys Ser Ala Pro Val Leu Ile His Thr Ser Lys Pro Phe Leu
 625 630 635 640

Pro Asp Ile Val Leu Thr Pro Leu Ser Asp Glu Leu Ser Asp Ile Asp
 645 650 655

Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser Gln
 660 665 670

Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu Gln
 675 680 685

Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe Thr
 690 695 700

Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu Pro
 705 710 715 720

Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp Leu
 725 730 735

Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser Thr
 740 745 750

Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys Asp
 755 760 765

Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp Asp
 770 775 780

Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser Ser
 785 790 795 800

Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe Gln
 805 810 815

501

Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr Gly
 820 825 830

Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln Ser
 835 840 845

Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp Ser
 850 855 860

Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala Thr
 865 870 875 880

Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly Ser
 885 890 895

Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met Glu
 900 905 910

Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu Gln
 915 920 925

Thr Pro Asp Asp Leu Gly Asn Ile Ser Lys Leu Asp Ile Tyr Leu Phe
 930 935 940

Ser Phe Arg Ala Ser Val Ser Gly Asp His Lys
 945 950 955

<210> 446
 <211> 1887
 <212> PRT
 <213> Homo sapien

<400> 446

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn

| 70 | | | | | | | | | | 75 | | | | | 80 | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|--|--|
| Lys | Glu | Asn | Gln | Glu | Arg | Gly | Phe | Ser | Phe | Leu | Phe | Ser | His | Phe | Lys | | | | | | |
| | | | | 85 | | | | | 90 | | | | | 95 | | | | | | | |
| Lys | Tyr | Tyr | Leu | Pro | Tyr | Ile | Phe | Pro | Asn | Ile | Cys | Lys | Glu | Asn | Ser | | | | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | | | | | |
| Leu | Tyr | His | Pro | Ile | Leu | Asp | Ile | Pro | Gln | Met | Arg | Pro | Lys | Pro | His | | | | | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | | | | | |
| Tyr | Val | Val | Ile | Lys | Lys | Asp | Ala | Glu | Thr | Asn | Glu | Ala | Ile | Tyr | Cys | | | | | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | | | | | | |
| Thr | Lys | Glu | Pro | Phe | Ile | Lys | Ala | Arg | Val | Ile | Val | Ile | Arg | Trp | Leu | | | | | | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | | | | | | |
| Val | Ser | Phe | Trp | Leu | Glu | Pro | Lys | Pro | His | Thr | Gly | Pro | His | Ile | Pro | | | | | | |
| | | | | 165 | | | | | 170 | | | | | 175 | | | | | | | |
| Gly | Met | Glu | Gly | Glu | Val | Leu | Pro | Lys | Asn | Ile | Gln | Arg | Ala | Ala | Ala | | | | | | |
| | | | 180 | | | | | 185 | | | | | 190 | | | | | | | | |
| Ser | Leu | Val | Ser | Arg | Glu | Glu | Ser | Lys | Asn | Asp | Asn | Ala | Asp | Lys | Thr | | | | | | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | | | | | |
| Asp | Arg | Thr | Thr | Glu | Pro | Glu | Gln | Ser | His | Ser | Asn | Thr | Ser | Thr | Leu | | | | | | |
| | 210 | | | | | 215 | | | | | 220 | | | | | | | | | | |
| Thr | Glu | Arg | Glu | Pro | Ser | Ser | Ser | Ser | Leu | Cys | Ser | Ile | Asp | Glu | Glu | | | | | | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | | | | | | |
| His | Leu | Thr | Asp | Ile | Glu | Ile | Val | Arg | Arg | Val | Phe | Ser | Ser | Lys | Arg | | | | | | |
| | | | | 245 | | | | | 250 | | | | | 255 | | | | | | | |
| Ser | Asn | Val | Asn | Phe | Val | Thr | Glu | Ile | Phe | Arg | Gln | Ala | Phe | Leu | Leu | | | | | | |
| | | | 260 | | | | | 265 | | | | | 270 | | | | | | | | |
| Pro | Ile | Cys | Glu | Ala | Ala | Ala | Met | Arg | Lys | Val | Val | Lys | Val | Tyr | Gln | | | | | | |
| | | 275 | | | | | 280 | | | | | 285 | | | | | | | | | |
| Glu | Trp | Ile | Gln | Gln | Glu | Glu | Lys | Pro | Leu | Phe | Met | Gln | Glu | Pro | Glu | | | | | | |
| | 290 | | | | | 295 | | | | | 300 | | | | | | | | | | |
| Glu | Ile | Val | Ile | Thr | Ser | Ser | Asp | Leu | Pro | Cys | Ile | Glu | Asn | Val | Thr | | | | | | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | | | | | | |

503

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Ser | Val | Asp | Lys | Ser | Phe | Ser | Arg | Gly | Trp | Ser | Arg | Asp | Gln | Pro |
| | | | | 565 | | | | | 570 | | | | | 575 | |
| Gly | Gln | Ala | Pro | Met | Arg | Gln | Arg | Ser | Ala | Thr | Thr | Thr | Gly | Ser | Pro |
| | | | 580 | | | | | 585 | | | | | 590 | | |
| Gly | Thr | Glu | Lys | Ala | Arg | Ser | Ile | Val | Arg | Gln | Lys | Thr | Val | Asp | Ile |
| | | 595 | | | | | 600 | | | | | 605 | | | |
| Asp | Asp | Ala | Gln | Ile | Leu | Pro | Arg | Ser | Thr | Arg | Val | Arg | His | Phe | Ser |
| | 610 | | | | | 615 | | | | | 620 | | | | |
| Gln | Ser | Glu | Glu | Thr | Gly | Asn | Glu | Val | Phe | Gly | Ala | Leu | Asn | Glu | Glu |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| Gln | Pro | Leu | Pro | Arg | Ser | Ser | Ser | Thr | Ser | Asp | Ile | Leu | Glu | Pro | Phe |
| | | | | 645 | | | | | 650 | | | | | 655 | |
| Thr | Val | Glu | Arg | Ala | Lys | Val | Asn | Lys | Glu | Asp | Met | Ser | Gln | Lys | Leu |
| | | | 660 | | | | | 665 | | | | | 670 | | |
| Pro | Pro | Leu | Asn | Ser | Asp | Ile | Gly | Gly | Ser | Ser | Ala | Asn | Val | Pro | Asp |
| | | 675 | | | | | 680 | | | | | 685 | | | |
| Leu | Met | Asp | Glu | Phe | Ile | Ala | Glu | Arg | Leu | Arg | Ser | Gly | Asn | Ala | Ser |
| | 690 | | | | | 695 | | | | | 700 | | | | |
| Thr | Met | Thr | Arg | Arg | Gly | Ser | Ser | Pro | Gly | Ser | Leu | Glu | Ile | Pro | Lys |
| 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| Asp | Leu | Pro | Asp | Ile | Leu | Asn | Lys | Gln | Asn | Gln | Met | Arg | Pro | Ile | Asp |
| | | | | 725 | | | | | 730 | | | | | 735 | |
| Asp | Pro | Gly | Val | Pro | Ser | Glu | Trp | Thr | Ser | Pro | Ala | Ser | Ala | Gly | Ser |
| | | | 740 | | | | | 745 | | | | | 750 | | |
| Ser | Asp | Leu | Ile | Ser | Ser | Asp | Ser | His | Ser | Asp | Ser | Phe | Ser | Ala | Phe |
| | | 755 | | | | | 760 | | | | | 765 | | | |
| Gln | Tyr | Asp | Gly | Arg | Lys | Phe | Asp | Asn | Phe | Gly | Phe | Gly | Thr | Asp | Thr |
| | 770 | | | | | 775 | | | | | 780 | | | | |
| Gly | Val | Thr | Ser | Ser | Ala | Asp | Val | Asp | Ser | Gly | Ser | Gly | His | His | Gln |
| 785 | | | | | 790 | | | | | 795 | | | | | 800 |

505

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 915 920 925

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 995 1000 1005

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe
 1010 1015 1020

Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile
 1025 1030 1035

Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu

506

| 1040 | 1045 | 1050 |
|-------------------------------------|-----------------------------|---------------------|
| Gly Leu Pro Gly Ala Thr Met 1055 | Leu Ile Met Asp Phe 1060 | Ile Val Ala 1065 |
| Ala Gly Arg Val Ala Ser Ser 1070 | Ala Phe Leu Asn Ala 1075 | Pro Arg Val 1080 |
| Glu Ala Gln Val Leu Leu Gly 1085 | Ser Leu Val Cys Phe 1090 | Pro Asn Leu 1095 |
| Tyr Cys Glu Leu Pro Ser Leu 1100 | His Pro Asn Ile Pro 1105 | Asp Val Ala 1110 |
| Val Ser Gln Phe Thr Asp Val 1115 | Lys Glu Leu Ile Ile 1120 | Lys Thr Val 1125 |
| Leu Ser Ser Ala Arg Asp Glu 1130 | Pro Ser Gly Pro Ala 1135 | Arg Cys Val 1140 |
| Ala Leu Cys Ser Leu Gly Ile 1145 | Trp Ile Cys Glu Glu 1150 | Leu Val His 1155 |
| Glu Ser His His Pro Gln Ile 1160 | Lys Glu Ala Leu Asn 1165 | Val Ile Cys 1170 |
| Val Ser Leu Lys Phe Thr Asn 1175 | Lys Thr Val Ala His 1180 | Val Ala Cys 1185 |
| Asn Met Leu His Met Leu Val 1190 | His Tyr Val Pro Arg 1195 | Leu Gln Ile 1200 |
| Tyr Gln Pro Asp Ser Pro Leu 1205 | Lys Ile Ile Gln Ile 1210 | Leu Ile Ala 1215 |
| Thr Ile Thr His Leu Leu Pro 1220 | Ser Thr Glu Ala Ser 1225 | Ser Tyr Glu 1230 |
| Met Asp Lys Arg Leu Val Val 1235 | Ser Leu Leu Leu Cys 1240 | Leu Leu Asp 1245 |
| Trp Ile Met Ala Leu Pro Leu 1250 | Lys Thr Leu Leu Gln 1255 | Pro Phe His 1260 |
| Ala Thr Gly Ala Glu Ser Asp 1265 | Lys Thr Glu Lys Ser 1270 | Val Leu Asn 1275 |

507

| | | |
|-----------------------------|---------------------|-------------|
| Cys Ile Tyr Lys Val Leu His | Gly Cys Val Tyr Gly | Ala Gln Cys |
| 1280 | 1285 | 1290 |
| Phe Ser Asn Pro Arg Tyr Phe | Pro Met Ser Leu Ser | Asp Leu Ala |
| 1295 | 1300 | 1305 |
| Ser Val Asp Tyr Asp Pro Phe | Met His Leu Glu Ser | Leu Lys Glu |
| 1310 | 1315 | 1320 |
| Pro Glu Pro Leu His Ser Pro | Asp Ser Glu Arg Ser | Ser Lys Leu |
| 1325 | 1330 | 1335 |
| Gln Pro Val Thr Glu Val Lys | Thr Gln Met Gln His | Gly Leu Ile |
| 1340 | 1345 | 1350 |
| Ser Ile Ala Ala Arg Thr Val | Ile Thr His Leu Val | Asn His Leu |
| 1355 | 1360 | 1365 |
| Gly His Tyr Pro Met Ser Gly | Gly Pro Ala Met Leu | Thr Ser Gln |
| 1370 | 1375 | 1380 |
| Val Cys Glu Asn His Asp Asn | His Tyr Ser Glu Ser | Thr Glu Leu |
| 1385 | 1390 | 1395 |
| Ser Pro Glu Leu Phe Glu Ser | Pro Asn Ile Gln Phe | Phe Val Leu |
| 1400 | 1405 | 1410 |
| Asn Asn Thr Thr Leu Val Ser | Cys Ile Gln Ile Arg | Ser Glu Glu |
| 1415 | 1420 | 1425 |
| Asn Met Pro Gly Gly Gly Leu | Ser Ala Gly Leu Ala | Ser Ala Asn |
| 1430 | 1435 | 1440 |
| Ser Asn Val Arg Ile Ile Val | Arg Asp Leu Ser Gly | Lys Tyr Ser |
| 1445 | 1450 | 1455 |
| Trp Asp Ser Ala Ile Leu Tyr | Gly Pro Pro Pro Val | Ser Gly Leu |
| 1460 | 1465 | 1470 |
| Ser Glu Pro Thr Ser Phe Met | Leu Ser Leu Ser His | Gln Glu Lys |
| 1475 | 1480 | 1485 |
| Pro Glu Glu Pro Pro Thr Ser | Asn Glu Cys Leu Glu | Asp Ile Thr |
| 1490 | 1495 | 1500 |

509

Val Ile Phe His Val Ser Thr Arg Met Pro Ser Asp Ser Asp Asp
 1730 1735 1740

Ser Leu Thr Lys Lys Leu Arg His Leu Gly Asn Asp Glu Val His
 1745 1750 1755

Ile Val Trp Ser Glu His Thr Arg Asp Tyr Arg Arg Gly Ile Ile
 1760 1765 1770

Pro Thr Glu Phe Gly Asp Val Leu Ile Val Ile Tyr Pro Met Lys
 1775 1780 1785

Asn His Met Phe Ser Ile Gln Ile Met Lys Lys Pro Glu Val Pro
 1790 1795 1800

Phe Phe Gly Pro Leu Phe Asp Gly Ala Ile Val Asn Gly Lys Val
 1805 1810 1815

Leu Pro Ile Met Val Arg Ala Thr Ala Ile Asn Ala Ser Arg Ala
 1820 1825 1830

Leu Lys Ser Leu Ile Pro Leu Tyr Gln Asn Phe Tyr Glu Glu Arg
 1835 1840 1845

Ala Arg Tyr Leu Gln Thr Ile Val Gln His His Leu Glu Pro Thr
 1850 1855 1860

Thr Phe Glu Asp Phe Ala Ala Gln Val Phe Ser Pro Ala Pro Tyr
 1865 1870 1875

His His Leu Pro Ser Asp Ala Asp His
 1880 1885

<210> 447

<211> 1455

<212> PRT

<213> Homo sapien

<400> 447

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 1 5 10 15

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 20 25 30

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 35 40 45

510

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
50 55 60

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
65 70 75 80

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
85 90 95

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
100 105 110

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
115 120 125

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
130 135 140

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
145 150 155 160

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
165 170 175

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
180 185 190

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
195 200 205

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
210 215 220

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
225 230 235 240

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
245 250 255

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
260 265 270

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
275 280 285

511

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 290 295 300

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 305 310 315 320

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 325 330 335

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 340 345 350

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 355 360 365

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 370 375 380

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 385 390 395 400

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 405 410 415

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 420 425 430

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 435 440 445

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 450 455 460

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 465 470 475 480

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 485 490 495

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 500 505 510

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 515 520 525

512

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 530 535 540

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 545 550 555 560

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 565 570 575

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe Tyr
 580 585 590

Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile Val Asn
 595 600 605

Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu Gly Leu Pro
 610 615 620

Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala Ala Gly Arg Val
 625 630 635 640

Ala Ser Ser Ala Phe Leu Asn Ala Pro Arg Val Glu Ala Gln Val Leu
 645 650 655

Leu Gly Ser Leu Val Cys Phe Pro Asn Leu Tyr Cys Glu Leu Pro Ser
 660 665 670

Leu His Pro Asn Ile Pro Asp Val Ala Val Ser Gln Phe Thr Asp Val
 675 680 685

Lys Glu Leu Ile Ile Lys Thr Val Leu Ser Ser Ala Arg Asp Glu Pro
 690 695 700

Ser Gly Pro Ala Arg Cys Val Ala Leu Cys Ser Leu Gly Ile Trp Ile
 705 710 715 720

Cys Glu Glu Leu Val His Glu Ser His His Pro Gln Ile Lys Glu Ala
 725 730 735

Leu Asn Val Ile Cys Val Ser Leu Lys Phe Thr Asn Lys Thr Val Ala
 740 745 750

His Val Ala Cys Asn Met Leu His Met Leu Val His Tyr Val Pro Arg
 755 760 765

Leu Gln Ile Tyr Gln Pro Asp Ser Pro Leu Lys Ile Ile Gln Ile Leu

513

770

775

780

Ile Ala Thr Ile Thr His Leu Leu Pro Ser Thr Glu Ala Ser Ser Tyr
 785 790 795 800

Glu Met Asp Lys Arg Leu Val Val Ser Leu Leu Leu Cys Leu Leu Asp
 805 810 815

Trp Ile Met Ala Leu Pro Leu Lys Thr Leu Leu Gln Pro Phe His Ala
 820 825 830

Thr Gly Ala Glu Ser Asp Lys Thr Glu Lys Ser Val Leu Asn Cys Ile
 835 840 845

Tyr Lys Val Leu His Gly Cys Val Tyr Gly Ala Gln Cys Phe Ser Asn
 850 855 860

Pro Arg Tyr Phe Pro Met Ser Leu Ser Asp Leu Ala Ser Val Asp Tyr
 865 870 875 880

Asp Pro Phe Met His Leu Glu Ser Leu Lys Glu Pro Glu Pro Leu His
 885 890 895

Ser Pro Asp Ser Glu Arg Ser Ser Lys Leu Gln Pro Val Thr Glu Val
 900 905 910

Lys Thr Gln Met Gln His Gly Leu Ile Ser Ile Ala Ala Arg Thr Val
 915 920 925

Ile Thr His Leu Val Asn His Leu Gly His Tyr Pro Met Ser Gly Gly
 930 935 940

Pro Ala Met Leu Thr Ser Gln Val Cys Glu Asn His Asp Asn His Tyr
 945 950 955 960

Ser Glu Ser Thr Glu Leu Ser Pro Glu Leu Phe Glu Ser Pro Asn Ile
 965 970 975

Gln Phe Phe Val Leu Asn Asn Thr Thr Leu Val Ser Cys Ile Gln Ile
 980 985 990

Arg Ser Glu Glu Asn Met Pro Gly Gly Gly Leu Ser Ala Gly Leu Ala
 995 1000 1005

Ser Ala Asn Ser Asn Val Arg Ile Ile Val Arg Asp Leu Ser Gly
 1010 1015 1020

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Lys | Tyr | Ser | Trp | Asp | Ser | Ala | Ile | Leu | Tyr | Gly | Pro | Pro | Pro | Val |
| 1025 | | | | | | 1030 | | | | | 1035 | | | |
| Ser | Gly | Leu | Ser | Glu | Pro | Thr | Ser | Phe | Met | Leu | Ser | Leu | Ser | His |
| 1040 | | | | | | 1045 | | | | | 1050 | | | |
| Gln | Glu | Lys | Pro | Glu | Glu | Pro | Pro | Thr | Ser | Asn | Glu | Cys | Leu | Glu |
| 1055 | | | | | | 1060 | | | | | 1065 | | | |
| Asp | Ile | Thr | Val | Lys | Asp | Gly | Leu | Ser | Leu | Gln | Phe | Lys | Arg | Phe |
| 1070 | | | | | | 1075 | | | | | 1080 | | | |
| Arg | Glu | Thr | Val | Pro | Thr | Trp | Asp | Thr | Ile | Arg | Asp | Glu | Glu | Asp |
| 1085 | | | | | | 1090 | | | | | 1095 | | | |
| Val | Leu | Asp | Glu | Leu | Leu | Gln | Tyr | Leu | Gly | Val | Thr | Ser | Pro | Glu |
| 1100 | | | | | | 1105 | | | | | 1110 | | | |
| Cys | Leu | Gln | Arg | Thr | Gly | Ile | Ser | Leu | Asn | Ile | Pro | Ala | Pro | Gln |
| 1115 | | | | | | 1120 | | | | | 1125 | | | |
| Pro | Val | Cys | Ile | Ser | Glu | Lys | Gln | Glu | Asn | Asp | Val | Ile | Asn | Ala |
| 1130 | | | | | | 1135 | | | | | 1140 | | | |
| Ile | Leu | Lys | Gln | His | Thr | Glu | Glu | Lys | Glu | Phe | Val | Glu | Lys | His |
| 1145 | | | | | | 1150 | | | | | 1155 | | | |
| Phe | Asn | Asp | Leu | Asn | Met | Lys | Ala | Val | Glu | Gln | Asp | Glu | Pro | Ile |
| 1160 | | | | | | 1165 | | | | | 1170 | | | |
| Pro | Gln | Lys | Pro | Gln | Ser | Ala | Phe | Tyr | Tyr | Cys | Arg | Leu | Leu | Leu |
| 1175 | | | | | | 1180 | | | | | 1185 | | | |
| Ser | Ile | Leu | Gly | Met | Asn | Ser | Trp | Asp | Lys | Arg | Arg | Ser | Phe | His |
| 1190 | | | | | | 1195 | | | | | 1200 | | | |
| Leu | Leu | Lys | Lys | Asn | Glu | Lys | Leu | Leu | Arg | Glu | Leu | Arg | Asn | Leu |
| 1205 | | | | | | 1210 | | | | | 1215 | | | |
| Asp | Ser | Arg | Gln | Cys | Arg | Glu | Thr | His | Lys | Ile | Ala | Val | Phe | Tyr |
| 1220 | | | | | | 1225 | | | | | 1230 | | | |
| Val | Ala | Glu | Gly | Gln | Glu | Asp | Lys | His | Ser | Ile | Leu | Thr | Asn | Thr |
| 1235 | | | | | | 1240 | | | | | 1245 | | | |

515

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Gly | Gly | Ser | Gln | Ala | Tyr | Glu | Asp | Phe | Val | Ala | Gly | Leu | Gly | Trp |
| 1250 | | | | | | 1255 | | | | | 1260 | | | |
| | | | | | | | | | | | | | | |
| Glu | Val | Asn | Leu | Thr | Asn | His | Cys | Gly | Phe | Met | Gly | Gly | Leu | Gln |
| 1265 | | | | | | 1270 | | | | | 1275 | | | |
| | | | | | | | | | | | | | | |
| Lys | Asn | Lys | Ser | Thr | Gly | Leu | Thr | Thr | Pro | Tyr | Phe | Ala | Thr | Ser |
| 1280 | | | | | | 1285 | | | | | 1290 | | | |
| | | | | | | | | | | | | | | |
| Thr | Val | Glu | Val | Ile | Phe | His | Val | Ser | Thr | Arg | Met | Pro | Ser | Asp |
| 1295 | | | | | | 1300 | | | | | 1305 | | | |
| | | | | | | | | | | | | | | |
| Ser | Asp | Asp | Ser | Leu | Thr | Lys | Lys | Leu | Arg | His | Leu | Gly | Asn | Asp |
| 1310 | | | | | | 1315 | | | | | 1320 | | | |
| | | | | | | | | | | | | | | |
| Glu | Val | His | Ile | Val | Trp | Ser | Glu | His | Thr | Arg | Asp | Tyr | Arg | Arg |
| 1325 | | | | | | 1330 | | | | | 1335 | | | |
| | | | | | | | | | | | | | | |
| Gly | Ile | Ile | Pro | Thr | Glu | Phe | Gly | Asp | Val | Leu | Ile | Val | Ile | Tyr |
| 1340 | | | | | | 1345 | | | | | 1350 | | | |
| | | | | | | | | | | | | | | |
| Pro | Met | Lys | Asn | His | Met | Phe | Ser | Ile | Gln | Ile | Met | Lys | Lys | Pro |
| 1355 | | | | | | 1360 | | | | | 1365 | | | |
| | | | | | | | | | | | | | | |
| Glu | Val | Pro | Phe | Phe | Gly | Pro | Leu | Phe | Asp | Gly | Ala | Ile | Val | Asn |
| 1370 | | | | | | 1375 | | | | | 1380 | | | |
| | | | | | | | | | | | | | | |
| Gly | Lys | Val | Leu | Pro | Ile | Met | Val | Arg | Ala | Thr | Ala | Ile | Asn | Ala |
| 1385 | | | | | | 1390 | | | | | 1395 | | | |
| | | | | | | | | | | | | | | |
| Ser | Arg | Ala | Leu | Lys | Ser | Leu | Ile | Pro | Leu | Tyr | Gln | Asn | Phe | Tyr |
| 1400 | | | | | | 1405 | | | | | 1410 | | | |
| | | | | | | | | | | | | | | |
| Glu | Glu | Arg | Ala | Arg | Tyr | Leu | Gln | Thr | Ile | Val | Gln | His | His | Leu |
| 1415 | | | | | | 1420 | | | | | 1425 | | | |
| | | | | | | | | | | | | | | |
| Glu | Pro | Thr | Thr | Phe | Glu | Asp | Phe | Ala | Ala | Gln | Val | Phe | Ser | Pro |
| 1430 | | | | | | 1435 | | | | | 1440 | | | |
| | | | | | | | | | | | | | | |
| Ala | Pro | Tyr | His | His | Leu | Pro | Ser | Asp | Ala | Asp | His | | | |
| 1445 | | | | | | 1450 | | | | | 1455 | | | |

<210> 448

<211> 1771

<212> PRT

<213> Homo sapien

516

<400> 448

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Arg Ala Ala Ala Ser Leu Val Ser
 65 70 75 80

Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr Asp Arg Thr Thr
 85 90 95

Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu Thr Glu Arg Glu
 100 105 110

Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu His Leu Thr Asp
 115 120 125

Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg Ser Asn Val Asn
 130 135 140

Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu Pro Ile Cys Glu
 145 150 155 160

Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln Glu Trp Ile Gln
 165 170 175

Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu Glu Ile Val Ile
 180 185 190

Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr Asp His Asp Ile
 195 200 205

Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn Gly Thr Asn Thr
 210 215 220

Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn Gly Ser Tyr Gln
 225 230 235 240

Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu Gln Asn Ile Arg
245 250 255

Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile Asn Ser Ser Asn
260 265 270

Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn Leu Leu Asp Glu
275 280 285

His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr Arg Tyr Met Val
290 295 300

Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln Met Leu Leu Val
305 310 315 320

Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro Ser Gln Ala Phe
325 330 335

Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala Gly Arg Leu Ala
340 345 350

Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile Lys Ala Asn Leu
355 360 365

Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu Leu Ser Val Leu
370 375 380

Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu Trp Ser Leu Thr
385 390 395 400

Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu Tyr Ser Leu Asp
405 410 415

Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln Lys Gln Lys Lys
420 425 430

His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys Val Ser Val Asp
435 440 445

Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro Gly Gln Ala Pro
450 455 460

Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro Gly Thr Glu Lys
465 470 475 480

518

Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile Asp Asp Ala Gln
 485 490 495

Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser Gln Ser Glu Glu
 500 505 510

Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu Gln Pro Leu Pro
 515 520 525

Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe Thr Val Glu Arg
 530 535 540

Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu Pro Pro Leu Asn
 545 550 555 560

Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp Leu Met Asp Glu
 565 570 575

Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser Thr Met Thr Arg
 580 585 590

Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys Asp Leu Pro Asp
 595 600 605

Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp Asp Pro Gly Val
 610 615 620

Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser Ser Asp Leu Ile
 625 630 635 640

Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe Gln Tyr Asp Gly
 645 650 655

Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr Gly Val Thr Ser
 660 665 670

Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln Ser Ala Glu Glu
 675 680 685

Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp Ser Glu Thr Ser
 690 695 700

Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala Thr Ile Thr Gly
 705 710 715 720

519

Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly Ser Arg Ser Gln
725 730 735

Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met Glu Gln Lys Asp
740 745 750

Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu Gln Thr Pro Asp
755 760 765

Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys Ser Val Met Ala
770 775 780

Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala Thr Val Met Trp
785 790 795 800

Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser Ile Met Asp Pro
805 810 815

Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu Leu Trp Gln Asn
820 825 830

Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr Asp Asn Leu Thr
835 840 845

Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg Ile Leu Thr Pro
850 855 860

Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr Lys Gln Gly Lys
865 870 875 880

Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys Arg Arg Gln Asp
885 890 895

Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe Tyr Asn Ile Met His
900 905 910

Cys Gly Leu Leu His Ile Asp Gln Asp Ile Val Asn Thr Ile Ile Lys
915 920 925

His Cys Ser Pro Gln Phe Phe Ser Leu Gly Leu Pro Gly Ala Thr Met
930 935 940

Leu Ile Met Asp Phe Ile Val Ala Ala Gly Arg Val Ala Ser Ser Ala
945 950 955 960

Phe Leu Asn Ala Pro Arg Val Glu Ala Gln Val Leu Leu Gly Ser Leu

520

965

970

975

Val Cys Phe Pro Asn Leu Tyr Cys Glu Leu Pro Ser Leu His Pro Asn
 980 985 990

Ile Pro Asp Val Ala Val Ser Gln Phe Thr Asp Val Lys Glu Leu Ile
 995 1000 1005

Ile Lys Thr Val Leu Ser Ser Ala Arg Asp Glu Pro Ser Gly Pro
 1010 1015 1020

Ala Arg Cys Val Ala Leu Cys Ser Leu Gly Ile Trp Ile Cys Glu
 1025 1030 1035

Glu Leu Val His Glu Ser His His Pro Gln Ile Lys Glu Ala Leu
 1040 1045 1050

Asn Val Ile Cys Val Ser Leu Lys Phe Thr Asn Lys Thr Val Ala
 1055 1060 1065

His Val Ala Cys Asn Met Leu His Met Leu Val His Tyr Val Pro
 1070 1075 1080

Arg Leu Gln Ile Tyr Gln Pro Asp Ser Pro Leu Lys Ile Ile Gln
 1085 1090 1095

Ile Leu Ile Ala Thr Ile Thr His Leu Leu Pro Ser Thr Glu Ala
 1100 1105 1110

Ser Ser Tyr Glu Met Asp Lys Arg Leu Val Val Ser Leu Leu Leu
 1115 1120 1125

Cys Leu Leu Asp Trp Ile Met Ala Leu Pro Leu Lys Thr Leu Leu
 1130 1135 1140

Gln Pro Phe His Ala Thr Gly Ala Glu Ser Asp Lys Thr Glu Lys
 1145 1150 1155

Ser Val Leu Asn Cys Ile Tyr Lys Val Leu His Gly Cys Val Tyr
 1160 1165 1170

Gly Ala Gln Cys Phe Ser Asn Pro Arg Tyr Phe Pro Met Ser Leu
 1175 1180 1185

Ser Asp Leu Ala Ser Val Asp Tyr Asp Pro Phe Met His Leu Glu
 1190 1195 1200

521

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Ser | Leu | Lys | Glu | Pro | Glu | Pro | Leu | His | Ser | Pro | Asp | Ser | Glu | Arg |
| 1205 | | | | | | 1210 | | | | | 1215 | | | |
| Ser | Ser | Lys | Leu | Gln | Pro | Val | Thr | Glu | Val | Lys | Thr | Gln | Met | Gln |
| 1220 | | | | | | 1225 | | | | | 1230 | | | |
| His | Gly | Leu | Ile | Ser | Ile | Ala | Ala | Arg | Thr | Val | Ile | Thr | His | Leu |
| 1235 | | | | | | 1240 | | | | | 1245 | | | |
| Val | Asn | His | Leu | Gly | His | Tyr | Pro | Met | Ser | Gly | Gly | Pro | Ala | Met |
| 1250 | | | | | | 1255 | | | | | 1260 | | | |
| Leu | Thr | Ser | Gln | Val | Cys | Glu | Asn | His | Asp | Asn | His | Tyr | Ser | Glu |
| 1265 | | | | | | 1270 | | | | | 1275 | | | |
| Ser | Thr | Glu | Leu | Ser | Pro | Glu | Leu | Phe | Glu | Ser | Pro | Asn | Ile | Gln |
| 1280 | | | | | | 1285 | | | | | 1290 | | | |
| Phe | Phe | Val | Leu | Asn | Asn | Thr | Thr | Leu | Val | Ser | Cys | Ile | Gln | Ile |
| 1295 | | | | | | 1300 | | | | | 1305 | | | |
| Arg | Ser | Glu | Glu | Asn | Met | Pro | Gly | Gly | Gly | Leu | Ser | Ala | Gly | Leu |
| 1310 | | | | | | 1315 | | | | | 1320 | | | |
| Ala | Ser | Ala | Asn | Ser | Asn | Val | Arg | Ile | Ile | Val | Arg | Asp | Leu | Ser |
| 1325 | | | | | | 1330 | | | | | 1335 | | | |
| Gly | Lys | Tyr | Ser | Trp | Asp | Ser | Ala | Ile | Leu | Tyr | Gly | Pro | Pro | Pro |
| 1340 | | | | | | 1345 | | | | | 1350 | | | |
| Val | Ser | Gly | Leu | Ser | Glu | Pro | Thr | Ser | Phe | Met | Leu | Ser | Leu | Ser |
| 1355 | | | | | | 1360 | | | | | 1365 | | | |
| His | Gln | Glu | Lys | Pro | Glu | Glu | Pro | Pro | Thr | Ser | Asn | Glu | Cys | Leu |
| 1370 | | | | | | 1375 | | | | | 1380 | | | |
| Glu | Asp | Ile | Thr | Val | Lys | Asp | Gly | Leu | Ser | Leu | Gln | Phe | Lys | Arg |
| 1385 | | | | | | 1390 | | | | | 1395 | | | |
| Phe | Arg | Glu | Thr | Val | Pro | Thr | Trp | Asp | Thr | Ile | Arg | Asp | Glu | Glu |
| 1400 | | | | | | 1405 | | | | | 1410 | | | |
| Asp | Val | Leu | Asp | Glu | Leu | Leu | Gln | Tyr | Leu | Gly | Val | Thr | Ser | Pro |
| 1415 | | | | | | 1420 | | | | | 1425 | | | |

522

| | | | | | | | | |
|---------|---------|---------|------|---------|---------|------|---------|-----|
| Glu Cys | Leu Gln | Arg Thr | Gly | Ile Ser | Leu Asn | Ile | Pro Ala | Pro |
| 1430 | | | 1435 | | | 1440 | | |
| Gln Pro | Val Cys | Ile Ser | Glu | Lys Gln | Glu Asn | Asp | Val Ile | Asn |
| 1445 | | | 1450 | | | 1455 | | |
| Ala Ile | Leu Lys | Gln His | Thr | Glu Glu | Lys Glu | Phe | Val Glu | Lys |
| 1460 | | | 1465 | | | 1470 | | |
| His Phe | Asn Asp | Leu Asn | Met | Lys Ala | Val Glu | Gln | Asp Glu | Pro |
| 1475 | | | 1480 | | | 1485 | | |
| Ile Pro | Gln Lys | Pro Gln | Ser | Ala Phe | Tyr Tyr | Cys | Arg Leu | Leu |
| 1490 | | | 1495 | | | 1500 | | |
| Leu Ser | Ile Leu | Gly Met | Asn | Ser Trp | Asp Lys | Arg | Arg Ser | Phe |
| 1505 | | | 1510 | | | 1515 | | |
| His Leu | Leu Lys | Lys Asn | Glu | Lys Leu | Leu Arg | Glu | Leu Arg | Asn |
| 1520 | | | 1525 | | | 1530 | | |
| Leu Asp | Ser Arg | Gln Cys | Arg | Glu Thr | His Lys | Ile | Ala Val | Phe |
| 1535 | | | 1540 | | | 1545 | | |
| Tyr Val | Ala Glu | Gly Gln | Glu | Asp Lys | His Ser | Ile | Leu Thr | Asn |
| 1550 | | | 1555 | | | 1560 | | |
| Thr Gly | Gly Ser | Gln Ala | Tyr | Glu Asp | Phe Val | Ala | Gly Leu | Gly |
| 1565 | | | 1570 | | | 1575 | | |
| Trp Glu | Val Asn | Leu Thr | Asn | His Cys | Gly Phe | Met | Gly Gly | Leu |
| 1580 | | | 1585 | | | 1590 | | |
| Gln Lys | Asn Lys | Ser Thr | Gly | Leu Thr | Thr Pro | Tyr | Phe Ala | Thr |
| 1595 | | | 1600 | | | 1605 | | |
| Ser Thr | Val Glu | Val Ile | Phe | His Val | Ser Thr | Arg | Met Pro | Ser |
| 1610 | | | 1615 | | | 1620 | | |
| Asp Ser | Asp Asp | Ser Leu | Thr | Lys Lys | Leu Arg | His | Leu Gly | Asn |
| 1625 | | | 1630 | | | 1635 | | |
| Asp Glu | Val His | Ile Val | Trp | Ser Glu | His Thr | Arg | Asp Tyr | Arg |
| 1640 | | | 1645 | | | 1650 | | |

523

Arg Gly Ile Ile Pro Thr Glu Phe Gly Asp Val Leu Ile Val Ile
 1655 1660 1665

Tyr Pro Met Lys Asn His Met Phe Ser Ile Gln Ile Met Lys Lys
 1670 1675 1680

Pro Glu Val Pro Phe Phe Gly Pro Leu Phe Asp Gly Ala Ile Val
 1685 1690 1695

Asn Gly Lys Val Leu Pro Ile Met Val Arg Ala Thr Ala Ile Asn
 1700 1705 1710

Ala Ser Arg Ala Leu Lys Ser Leu Ile Pro Leu Tyr Gln Asn Phe
 1715 1720 1725

Tyr Glu Glu Arg Ala Arg Tyr Leu Gln Thr Ile Val Gln His His
 1730 1735 1740

Leu Glu Pro Thr Thr Phe Glu Asp Phe Ala Ala Gln Val Phe Ser
 1745 1750 1755

Pro Ala Pro Tyr His His Leu Pro Ser Asp Ala Asp His
 1760 1765 1770

<210> 449

<211> 1403

<212> PRT

<213> Homo sapien

<400> 449

Met Lys Ile Ala Thr Lys Lys Arg Asn Ser Val His Val Thr Phe Arg
 1 5 10 15

Pro Ser Thr Glu Ser Val Gln Phe Tyr Asn Pro Leu Glu Asn Lys Glu
 20 25 30

Ala Pro Trp Lys Met Arg Leu Arg Lys Leu Gly Gly Phe Ser Ser Gly
 35 40 45

Ser Ser Asn Ser Ser Thr Ser Asn Thr His Thr Ser Thr Asn Ser Ala
 50 55 60

Thr Glu Leu Val Lys Pro Gly Val Tyr Arg Pro Leu Asp Thr Leu Gly
 65 70 75 80

Thr Ala Ser Val Ser Ser Lys Thr Val Lys Glu Ser Thr Glu Ile Pro
 85 90 95

524

Thr Thr Ile Leu Gln Lys Glu Gly Ile Ala Ser Ser Gln Leu Gly Ser
 100 105 110

Arg Ser Thr Leu Arg Ser Ser Ser His Glu Ala Gly Leu Gln Gln Gly
 115 120 125

Ser Leu Gly Gly Val Tyr Lys Thr Val Val His Ala Leu Ser Lys Pro
 130 135 140

Lys Ala Asn Val Ser Pro Gln Arg Gln Asn Arg Met Pro Pro Glu Ala
 145 150 155 160

Pro Leu Arg Asp Leu Tyr Ser His Val Met Gly Tyr Phe Gly Arg Lys
 165 170 175

Ala Ala Val Asn Lys Glu Asp Met Ser Gln Lys Leu Pro Pro Leu Asn
 180 185 190

Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp Leu Met Asp Glu
 195 200 205

Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser Thr Met Thr Arg
 210 215 220

Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys Asp Leu Pro Asp
 225 230 235 240

Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp Asp Pro Gly Val
 245 250 255

Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser Ser Asp Leu Ile
 260 265 270

Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe Gln Tyr Asp Gly
 275 280 285

Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr Gly Val Thr Ser
 290 295 300

Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln Ser Ala Glu Glu
 305 310 315 320

Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp Ser Glu Thr Ser
 325 330 335

525

Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala Thr Ile Thr Gly
 340 345 350

Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly Ser Arg Ser Gln
 355 360 365

Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met Glu Gln Lys Asp
 370 375 380

Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu Gln Thr Pro Asp
 385 390 395 400

Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys Ser Val Met Ala
 405 410 415

Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala Thr Val Met Trp
 420 425 430

Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser Ile Met Asp Pro
 435 440 445

Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu Leu Trp Gln Asn
 450 455 460

Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr Asp Asn Leu Thr
 465 470 475 480

Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg Ile Leu Thr Pro
 485 490 495

Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr Lys Gln Gly Lys
 500 505 510

Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys Arg Arg Gln Asp
 515 520 525

Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe Tyr Asn Ile Met His
 530 535 540

Cys Gly Leu Leu His Ile Asp Gln Asp Ile Val Asn Thr Ile Ile Lys
 545 550 555 560

His Cys Ser Pro Gln Phe Phe Ser Leu Gly Leu Pro Gly Ala Thr Met
 565 570 575

526

Leu Ile Met Asp Phe Ile Val Ala Ala Gly Arg Val Ala Ser Ser Ala
 580 585 590

Phe Leu Asn Ala Pro Arg Val Glu Ala Gln Val Leu Leu Gly Ser Leu
 595 600 605

Val Cys Phe Pro Asn Leu Tyr Cys Glu Leu Pro Ser Leu His Pro Asn
 610 615 620

Ile Pro Asp Val Ala Val Ser Gln Phe Thr Asp Val Lys Glu Leu Ile
 625 630 635 640

Ile Lys Thr Val Leu Ser Ser Ala Arg Asp Glu Pro Ser Gly Pro Ala
 645 650 655

Arg Cys Val Ala Leu Cys Ser Leu Gly Ile Trp Ile Cys Glu Glu Leu
 660 665 670

Val His Glu Ser His His Pro Gln Ile Lys Glu Ala Leu Asn Val Ile
 675 680 685

Cys Val Ser Leu Lys Phe Thr Asn Lys Thr Val Ala His Val Ala Cys
 690 695 700

Asn Met Leu His Met Leu Val His Tyr Val Pro Arg Leu Gln Ile Tyr
 705 710 715 720

Gln Pro Asp Ser Pro Leu Lys Ile Ile Gln Ile Leu Ile Ala Thr Ile
 725 730 735

Thr His Leu Leu Pro Ser Thr Glu Ala Ser Ser Tyr Glu Met Asp Lys
 740 745 750

Arg Leu Val Val Ser Leu Leu Leu Cys Leu Leu Asp Trp Ile Met Ala
 755 760 765

Leu Pro Leu Lys Thr Leu Leu Gln Pro Phe His Ala Thr Gly Ala Glu
 770 775 780

Ser Asp Lys Thr Glu Lys Ser Val Leu Asn Cys Ile Tyr Lys Val Leu
 785 790 795 800

His Gly Cys Val Tyr Gly Ala Gln Cys Phe Ser Asn Pro Arg Tyr Phe
 805 810 815

Pro Met Ser Leu Ser Asp Leu Ala Ser Val Asp Tyr Asp Pro Phe Met

527

820

825

830

His Leu Glu Ser Leu Lys Glu Pro Glu Pro Leu His Ser Pro Asp Ser
835 840 845

Glu Arg Ser Ser Lys Leu Gln Pro Val Thr Glu Val Lys Thr Gln Met
850 855 860

Gln His Gly Leu Ile Ser Ile Ala Ala Arg Thr Val Ile Thr His Leu
865 870 875 880

Val Asn His Leu Gly His Tyr Pro Met Ser Gly Gly Pro Ala Met Leu
885 890 895

Thr Ser Gln Val Cys Glu Asn His Asp Asn His Tyr Ser Glu Ser Thr
900 905 910

Glu Leu Ser Pro Glu Leu Phe Glu Ser Pro Asn Ile Gln Phe Phe Val
915 920 925

Leu Asn Asn Thr Thr Leu Val Ser Cys Ile Gln Ile Arg Ser Glu Glu
930 935 940

Asn Met Pro Gly Gly Gly Leu Ser Ala Gly Leu Ala Ser Ala Asn Ser
945 950 955 960

Asn Val Arg Ile Ile Val Arg Asp Leu Ser Gly Lys Tyr Ser Trp Asp
965 970 975

Ser Ala Ile Leu Tyr Gly Pro Pro Pro Val Ser Gly Leu Ser Glu Pro
980 985 990

Thr Ser Phe Met Leu Ser Leu Ser His Gln Glu Lys Pro Glu Glu Pro
995 1000 1005

Pro Thr Ser Asn Glu Cys Leu Glu Asp Ile Thr Val Lys Asp Gly
1010 1015 1020

Leu Ser Leu Gln Phe Lys Arg Phe Arg Glu Thr Val Pro Thr Trp
1025 1030 1035

Asp Thr Ile Arg Asp Glu Glu Asp Val Leu Asp Glu Leu Leu Gln
1040 1045 1050

Tyr Leu Gly Val Thr Ser Pro Glu Cys Leu Gln Arg Thr Gly Ile
1055 1060 1065

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Ser | Leu | Asn | Ile | Pro | Ala | Pro | Gln | Pro | Val | Cys | Ile | Ser | Glu | Lys |
| 1070 | | | | | | 1075 | | | | | 1080 | | | |
| Gln | Glu | Asn | Asp | Val | Ile | Asn | Ala | Ile | Leu | Lys | Gln | His | Thr | Glu |
| 1085 | | | | | | 1090 | | | | | 1095 | | | |
| Glu | Lys | Glu | Phe | Val | Glu | Lys | His | Phe | Asn | Asp | Leu | Asn | Met | Lys |
| 1100 | | | | | | 1105 | | | | | 1110 | | | |
| Ala | Val | Glu | Gln | Asp | Glu | Pro | Ile | Pro | Gln | Lys | Pro | Gln | Ser | Ala |
| 1115 | | | | | | 1120 | | | | | 1125 | | | |
| Phe | Tyr | Tyr | Cys | Arg | Leu | Leu | Leu | Ser | Ile | Leu | Gly | Met | Asn | Ser |
| 1130 | | | | | | 1135 | | | | | 1140 | | | |
| Trp | Asp | Lys | Arg | Arg | Ser | Phe | His | Leu | Leu | Lys | Lys | Asn | Glu | Lys |
| 1145 | | | | | | 1150 | | | | | 1155 | | | |
| Leu | Leu | Arg | Glu | Leu | Arg | Asn | Leu | Asp | Ser | Arg | Gln | Cys | Arg | Glu |
| 1160 | | | | | | 1165 | | | | | 1170 | | | |
| Thr | His | Lys | Ile | Ala | Val | Phe | Tyr | Val | Ala | Glu | Gly | Gln | Glu | Asp |
| 1175 | | | | | | 1180 | | | | | 1185 | | | |
| Lys | His | Ser | Ile | Leu | Thr | Asn | Thr | Gly | Gly | Ser | Gln | Ala | Tyr | Glu |
| 1190 | | | | | | 1195 | | | | | 1200 | | | |
| Asp | Phe | Val | Ala | Gly | Leu | Gly | Trp | Glu | Val | Asn | Leu | Thr | Asn | His |
| 1205 | | | | | | 1210 | | | | | 1215 | | | |
| Cys | Gly | Phe | Met | Gly | Gly | Leu | Gln | Lys | Asn | Lys | Ser | Thr | Gly | Leu |
| 1220 | | | | | | 1225 | | | | | 1230 | | | |
| Thr | Thr | Pro | Tyr | Phe | Ala | Thr | Ser | Thr | Val | Glu | Val | Ile | Phe | His |
| 1235 | | | | | | 1240 | | | | | 1245 | | | |
| Val | Ser | Thr | Arg | Met | Pro | Ser | Asp | Ser | Asp | Asp | Ser | Leu | Thr | Lys |
| 1250 | | | | | | 1255 | | | | | 1260 | | | |
| Lys | Leu | Arg | His | Leu | Gly | Asn | Asp | Glu | Val | His | Ile | Val | Trp | Ser |
| 1265 | | | | | | 1270 | | | | | 1275 | | | |
| Glu | His | Thr | Arg | Asp | Tyr | Arg | Arg | Gly | Ile | Ile | Pro | Thr | Glu | Phe |
| 1280 | | | | | | 1285 | | | | | 1290 | | | |

529

Gly Asp Val Leu Ile Val Ile Tyr Pro Met Lys Asn His Met Phe
 1295 1300 1305

Ser Ile Gln Ile Met Lys Lys Pro Glu Val Pro Phe Phe Gly Pro
 1310 1315 1320

Leu Phe Asp Gly Ala Ile Val Asn Gly Lys Val Leu Pro Ile Met
 1325 1330 1335

Val Arg Ala Thr Ala Ile Asn Ala Ser Arg Ala Leu Lys Ser Leu
 1340 1345 1350

Ile Pro Leu Tyr Gln Asn Phe Tyr Glu Glu Arg Ala Arg Tyr Leu
 1355 1360 1365

Gln Thr Ile Val Gln His His Leu Glu Pro Thr Thr Phe Glu Asp
 1370 1375 1380

Phe Ala Ala Gln Val Phe Ser Pro Ala Pro Tyr His His Leu Pro
 1385 1390 1395

Ser Asp Ala Asp His
 1400

<210> 450
 <211> 1909
 <212> PRT
 <213> Homo sapien

<400> 450

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys

530

85

90

95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

531

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

532

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
 675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

533

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 915 920 925

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 995 1000 1005

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe
 1010 1015 1020

Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile
 1025 1030 1035

Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu
 1040 1045 1050

Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala

534

| | | | | |
|-----------------------------|---------------------|-------------|--|------|
| 1055 | | 1060 | | 1065 |
| Ala Gly Arg Val Ala Ser Ser | Ala Phe Leu Asn Ala | Pro Arg Val | | |
| 1070 | 1075 | 1080 | | |
| Glu Ala Gln Val Leu Leu Gly | Ser Leu Val Cys Phe | Pro Asn Leu | | |
| 1085 | 1090 | 1095 | | |
| Tyr Cys Glu Leu Pro Ser Leu | His Pro Asn Ile Pro | Asp Val Ala | | |
| 1100 | 1105 | 1110 | | |
| Val Ser Gln Phe Thr Asp Val | Lys Glu Leu Ile Ile | Lys Thr Val | | |
| 1115 | 1120 | 1125 | | |
| Leu Ser Ser Ala Arg Asp Glu | Pro Ser Gly Pro Ala | Arg Cys Val | | |
| 1130 | 1135 | 1140 | | |
| Ala Leu Cys Ser Leu Gly Ile | Trp Ile Cys Glu Glu | Leu Val His | | |
| 1145 | 1150 | 1155 | | |
| Glu Ser His His Pro Gln Ile | Lys Glu Ala Leu Asn | Val Ile Cys | | |
| 1160 | 1165 | 1170 | | |
| Val Ser Leu Lys Phe Thr Asn | Lys Thr Val Ala His | Val Ala Cys | | |
| 1175 | 1180 | 1185 | | |
| Asn Met Leu His Met Leu Val | His Tyr Val Pro Arg | Leu Gln Ile | | |
| 1190 | 1195 | 1200 | | |
| Tyr Gln Pro Asp Ser Pro Leu | Lys Ile Ile Gln Ile | Leu Ile Ala | | |
| 1205 | 1210 | 1215 | | |
| Thr Ile Thr His Leu Leu Pro | Ser Thr Glu Ala Ser | Ser Tyr Glu | | |
| 1220 | 1225 | 1230 | | |
| Met Asp Lys Arg Leu Val Val | Ser Leu Leu Leu Cys | Leu Leu Asp | | |
| 1235 | 1240 | 1245 | | |
| Trp Ile Met Ala Leu Pro Leu | Lys Thr Leu Leu Gln | Pro Phe His | | |
| 1250 | 1255 | 1260 | | |
| Ala Thr Gly Ala Glu Ser Asp | Lys Thr Glu Lys Ser | Val Leu Asn | | |
| 1265 | 1270 | 1275 | | |
| Cys Ile Tyr Lys Val Leu His | Gly Cys Val Tyr Gly | Ala Gln Cys | | |
| 1280 | 1285 | 1290 | | |

535

| | | | |
|---|------|------|------|
| Phe Ser Asn Pro Arg Tyr Phe Pro Met Ser Leu Ser Asp Leu Ala | 1295 | 1300 | 1305 |
| Ser Val Asp Tyr Asp Pro Phe Met His Leu Glu Ser Leu Lys Glu | 1310 | 1315 | 1320 |
| Pro Glu Pro Leu His Ser Pro Asp Ser Glu Arg Ser Ser Lys Leu | 1325 | 1330 | 1335 |
| Gln Pro Val Thr Glu Val Lys Thr Gln Met Gln His Gly Leu Ile | 1340 | 1345 | 1350 |
| Ser Ile Ala Ala Arg Thr Val Ile Thr His Leu Val Asn His Leu | 1355 | 1360 | 1365 |
| Gly His Tyr Pro Met Ser Gly Gly Pro Ala Met Leu Thr Ser Gln | 1370 | 1375 | 1380 |
| Val Cys Glu Asn His Asp Asn His Tyr Ser Glu Ser Thr Glu Leu | 1385 | 1390 | 1395 |
| Ser Pro Glu Leu Phe Glu Ser Pro Asn Ile Gln Phe Phe Val Leu | 1400 | 1405 | 1410 |
| Asn Asn Thr Thr Leu Val Ser Cys Ile Gln Ile Arg Ser Glu Glu | 1415 | 1420 | 1425 |
| Asn Met Pro Gly Gly Gly Leu Ser Ala Gly Leu Ala Ser Ala Asn | 1430 | 1435 | 1440 |
| Ser Asn Val Arg Ile Ile Val Arg Asp Leu Ser Gly Lys Tyr Ser | 1445 | 1450 | 1455 |
| Trp Asp Ser Ala Ile Leu Tyr Gly Pro Pro Pro Val Ser Gly Leu | 1460 | 1465 | 1470 |
| Ser Glu Pro Thr Ser Phe Met Leu Ser Leu Ser His Gln Glu Lys | 1475 | 1480 | 1485 |
| Pro Glu Glu Pro Pro Thr Ser Asn Glu Cys Leu Glu Asp Ile Thr | 1490 | 1495 | 1500 |
| Val Lys Asp Gly Leu Ser Leu Gln Phe Lys Arg Phe Arg Glu Thr | 1505 | 1510 | 1515 |

536

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Val | Pro | Thr | Trp | Asp | Thr | Ile | Arg | Asp | Glu | Glu | Asp | Val | Leu | Asp |
| 1520 | | | | | | 1525 | | | | | 1530 | | | |
| Glu | Leu | Leu | Gln | Tyr | Leu | Gly | Val | Thr | Ser | Pro | Glu | Cys | Leu | Gln |
| 1535 | | | | | | 1540 | | | | | 1545 | | | |
| Arg | Thr | Gly | Ile | Ser | Leu | Asn | Ile | Pro | Ala | Pro | Gln | Pro | Val | Cys |
| 1550 | | | | | | 1555 | | | | | 1560 | | | |
| Ile | Ser | Glu | Lys | Gln | Glu | Asn | Asp | Val | Ile | Asn | Ala | Ile | Leu | Lys |
| 1565 | | | | | | 1570 | | | | | 1575 | | | |
| Gln | His | Thr | Glu | Glu | Lys | Glu | Phe | Val | Glu | Lys | His | Phe | Asn | Asp |
| 1580 | | | | | | 1585 | | | | | 1590 | | | |
| Leu | Asn | Met | Lys | Ala | Val | Glu | Gln | Asp | Glu | Pro | Ile | Pro | Gln | Lys |
| 1595 | | | | | | 1600 | | | | | 1605 | | | |
| Pro | Gln | Ser | Ala | Phe | Tyr | Tyr | Cys | Arg | Leu | Leu | Leu | Ser | Ile | Leu |
| 1610 | | | | | | 1615 | | | | | 1620 | | | |
| Gly | Met | Asn | Ser | Trp | Asp | Lys | Arg | Arg | Ser | Phe | His | Leu | Leu | Lys |
| 1625 | | | | | | 1630 | | | | | 1635 | | | |
| Lys | Asn | Glu | Lys | Leu | Leu | Arg | Glu | Leu | Arg | Asn | Leu | Asp | Ser | Arg |
| 1640 | | | | | | 1645 | | | | | 1650 | | | |
| Gln | Cys | Arg | Glu | Thr | His | Lys | Ile | Ala | Val | Phe | Tyr | Val | Ala | Glu |
| 1655 | | | | | | 1660 | | | | | 1665 | | | |
| Gly | Gln | Glu | Asp | Lys | His | Ser | Ile | Leu | Thr | Asn | Thr | Gly | Gly | Ser |
| 1670 | | | | | | 1675 | | | | | 1680 | | | |
| Gln | Ala | Tyr | Glu | Asp | Phe | Val | Ala | Gly | Leu | Gly | Trp | Glu | Val | Asn |
| 1685 | | | | | | 1690 | | | | | 1695 | | | |
| Leu | Thr | Asn | His | Cys | Gly | Phe | Met | Gly | Gly | Leu | Gln | Lys | Asn | Lys |
| 1700 | | | | | | 1705 | | | | | 1710 | | | |
| Ser | Thr | Gly | Leu | Thr | Thr | Pro | Tyr | Phe | Ala | Thr | Ser | Thr | Val | Glu |
| 1715 | | | | | | 1720 | | | | | 1725 | | | |
| Val | Ile | Phe | His | Val | Ser | Thr | Arg | Met | Pro | Ser | Asp | Ser | Asp | Asp |
| 1730 | | | | | | 1735 | | | | | 1740 | | | |

537

Ser Leu Thr Lys Lys Ile Gln Val Tyr Asp Thr Tyr Val Phe Leu
 1745 1750 1755

Leu Ser Glu Glu Leu Val Leu Thr Phe Leu Glu Glu Leu Arg His
 1760 1765 1770

Leu Gly Asn Asp Glu Val His Ile Val Trp Ser Glu His Thr Arg
 1775 1780 1785

Asp Tyr Arg Arg Gly Ile Ile Pro Thr Glu Phe Gly Asp Val Leu
 1790 1795 1800

Ile Val Ile Tyr Pro Met Lys Asn His Met Phe Ser Ile Gln Ile
 1805 1810 1815

Met Lys Lys Pro Glu Val Pro Phe Phe Gly Pro Leu Phe Asp Gly
 1820 1825 1830

Ala Ile Val Asn Gly Lys Val Leu Pro Ile Met Val Arg Ala Thr
 1835 1840 1845

Ala Ile Asn Ala Ser Arg Ala Leu Lys Ser Leu Ile Pro Leu Tyr
 1850 1855 1860

Gln Asn Phe Tyr Glu Glu Arg Ala Arg Tyr Leu Gln Thr Ile Val
 1865 1870 1875

Gln His His Leu Glu Pro Thr Thr Phe Glu Asp Phe Ala Ala Gln
 1880 1885 1890

Val Phe Ser Pro Ala Pro Tyr His His Leu Pro Ser Asp Ala Asp
 1895 1900 1905

His

<210> 451
 <211> 1704
 <212> PRT
 <213> Homo sapien

<400> 451

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

538

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

539

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

540

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
 675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe

541

755

760

765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 915 920 925

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 995 1000 1005

542

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Arg | Arg | Gln | Asp | Val | Ser | Pro | Asn | Arg | Asp | Phe | Leu | Thr | His | Phe |
| 1010 | | | | | | 1015 | | | | | 1020 | | | |
| Tyr | Asn | Ile | Met | His | Cys | Gly | Leu | Leu | His | Ile | Asp | Gln | Asp | Ile |
| 1025 | | | | | | 1030 | | | | | 1035 | | | |
| Val | Asn | Thr | Ile | Ile | Lys | His | Cys | Ser | Pro | Gln | Phe | Phe | Ser | Leu |
| 1040 | | | | | | 1045 | | | | | 1050 | | | |
| Gly | Leu | Pro | Gly | Ala | Thr | Met | Leu | Ile | Met | Asp | Phe | Ile | Val | Ala |
| 1055 | | | | | | 1060 | | | | | 1065 | | | |
| Ala | Gly | Arg | Val | Ala | Ser | Ser | Ala | Phe | Leu | Asn | Ala | Pro | Arg | Val |
| 1070 | | | | | | 1075 | | | | | 1080 | | | |
| Glu | Ala | Gln | Val | Leu | Leu | Gly | Ser | Leu | Val | Cys | Phe | Pro | Asn | Leu |
| 1085 | | | | | | 1090 | | | | | 1095 | | | |
| Tyr | Cys | Glu | Leu | Pro | Ser | Leu | His | Pro | Asn | Ile | Pro | Asp | Val | Ala |
| 1100 | | | | | | 1105 | | | | | 1110 | | | |
| Val | Ser | Gln | Phe | Thr | Asp | Val | Lys | Glu | Leu | Ile | Ile | Lys | Thr | Val |
| 1115 | | | | | | 1120 | | | | | 1125 | | | |
| Leu | Ser | Ser | Ala | Arg | Asp | Glu | Pro | Ser | Gly | Pro | Ala | Arg | Cys | Val |
| 1130 | | | | | | 1135 | | | | | 1140 | | | |
| Ala | Leu | Cys | Ser | Leu | Gly | Ile | Trp | Ile | Cys | Glu | Glu | Leu | Val | His |
| 1145 | | | | | | 1150 | | | | | 1155 | | | |
| Glu | Ser | His | His | Pro | Gln | Ile | Lys | Glu | Ala | Leu | Asn | Val | Ile | Cys |
| 1160 | | | | | | 1165 | | | | | 1170 | | | |
| Val | Ser | Leu | Lys | Phe | Thr | Asn | Lys | Thr | Val | Ala | His | Val | Ala | Cys |
| 1175 | | | | | | 1180 | | | | | 1185 | | | |
| Asn | Met | Leu | His | Met | Leu | Val | His | Tyr | Val | Pro | Arg | Leu | Gln | Ile |
| 1190 | | | | | | 1195 | | | | | 1200 | | | |
| Tyr | Gln | Pro | Asp | Ser | Pro | Leu | Lys | Ile | Ile | Gln | Ile | Leu | Ile | Ala |
| 1205 | | | | | | 1210 | | | | | 1215 | | | |
| Thr | Ile | Thr | His | Leu | Leu | Pro | Ser | Thr | Glu | Ala | Ser | Ser | Tyr | Glu |
| 1220 | | | | | | 1225 | | | | | 1230 | | | |

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| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Met | Asp | Lys | Arg | Leu | Val | Val | Ser | Leu | Leu | Leu | Cys | Leu | Leu | Asp |
| 1235 | | | | | | 1240 | | | | | 1245 | | | |
| Trp | Ile | Met | Ala | Leu | Pro | Leu | Lys | Thr | Leu | Leu | Gln | Pro | Phe | His |
| 1250 | | | | | | 1255 | | | | | 1260 | | | |
| Ala | Thr | Gly | Ala | Glu | Ser | Asp | Lys | Thr | Glu | Lys | Ser | Val | Leu | Asn |
| 1265 | | | | | | 1270 | | | | | 1275 | | | |
| Cys | Ile | Tyr | Lys | Val | Leu | His | Gly | Cys | Val | Tyr | Gly | Ala | Gln | Cys |
| 1280 | | | | | | 1285 | | | | | 1290 | | | |
| Phe | Ser | Asn | Pro | Arg | Tyr | Phe | Pro | Met | Ser | Leu | Ser | Asp | Leu | Ala |
| 1295 | | | | | | 1300 | | | | | 1305 | | | |
| Ser | Val | Asp | Tyr | Asp | Pro | Phe | Met | His | Leu | Glu | Ser | Leu | Lys | Glu |
| 1310 | | | | | | 1315 | | | | | 1320 | | | |
| Pro | Glu | Pro | Leu | His | Ser | Pro | Asp | Ser | Glu | Arg | Ser | Ser | Lys | Leu |
| 1325 | | | | | | 1330 | | | | | 1335 | | | |
| Gln | Pro | Val | Thr | Glu | Val | Lys | Thr | Gln | Met | Gln | His | Gly | Leu | Ile |
| 1340 | | | | | | 1345 | | | | | 1350 | | | |
| Ser | Ile | Ala | Ala | Arg | Thr | Val | Ile | Thr | His | Leu | Val | Asn | His | Leu |
| 1355 | | | | | | 1360 | | | | | 1365 | | | |
| Gly | His | Tyr | Pro | Met | Ser | Gly | Gly | Pro | Ala | Met | Leu | Thr | Ser | Gln |
| 1370 | | | | | | 1375 | | | | | 1380 | | | |
| Val | Cys | Glu | Asn | His | Asp | Asn | His | Tyr | Ser | Glu | Ser | Thr | Glu | Leu |
| 1385 | | | | | | 1390 | | | | | 1395 | | | |
| Ser | Pro | Glu | Leu | Phe | Glu | Ser | Pro | Asn | Ile | Gln | Phe | Phe | Val | Leu |
| 1400 | | | | | | 1405 | | | | | 1410 | | | |
| Asn | Asn | Thr | Thr | Leu | Val | Ser | Cys | Ile | Gln | Ile | Arg | Ser | Glu | Glu |
| 1415 | | | | | | 1420 | | | | | 1425 | | | |
| Asn | Met | Pro | Gly | Gly | Gly | Leu | Ser | Ala | Gly | Leu | Ala | Ser | Ala | Asn |
| 1430 | | | | | | 1435 | | | | | 1440 | | | |
| Ser | Asn | Val | Arg | Ile | Ile | Val | Arg | Asp | Leu | Ser | Gly | Lys | Tyr | Ser |
| 1445 | | | | | | 1450 | | | | | 1455 | | | |

544

| | | | |
|-----------------|-----------------------------|-----------------------------|-------------|
| Trp Asp 1460 | Ser Ala Ile Leu Tyr 1465 | Gly Pro Pro Pro Val 1470 | Ser Gly Leu |
| Ser Glu 1475 | Pro Thr Ser Phe Met 1480 | Leu Ser Leu Ser His 1485 | Gln Glu Lys |
| Pro Glu 1490 | Glu Pro Pro Thr Ser 1495 | Asn Glu Cys Leu Glu 1500 | Asp Ile Thr |
| Val Lys 1505 | Asp Gly Leu Ser Leu 1510 | Gln Phe Lys Arg Phe 1515 | Arg Glu Thr |
| Val Pro 1520 | Thr Trp Asp Thr Ile 1525 | Arg Asp Glu Glu Asp 1530 | Val Leu Asp |
| Glu Leu 1535 | Leu Gln Tyr Leu Gly 1540 | Val Thr Ser Pro Glu 1545 | Cys Leu Gln |
| Arg Thr 1550 | Gly Ile Ser Leu Asn 1555 | Ile Pro Ala Pro Gln 1560 | Pro Val Cys |
| Ile Ser 1565 | Glu Lys Gln Glu Asn 1570 | Asp Val Ile Asn Ala 1575 | Ile Leu Lys |
| Gln His 1580 | Thr Glu Glu Lys Glu 1585 | Phe Val Glu Lys His 1590 | Phe Asn Asp |
| Leu Asn 1595 | Met Lys Ala Val Glu 1600 | Gln Asp Glu Pro Ile 1605 | Pro Gln Lys |
| Pro Gln 1610 | Ser Ala Phe Tyr Tyr 1615 | Cys Arg Leu Leu Leu 1620 | Ser Ile Leu |
| Gly Met 1625 | Asn Ser Trp Asp Lys 1630 | Arg Arg Ser Phe His 1635 | Leu Leu Lys |
| Lys Asn 1640 | Glu Lys Leu Leu Arg 1645 | Glu Leu Arg Asn Leu 1650 | Asp Ser Arg |
| Gln Cys 1655 | Arg Glu Thr His Lys 1660 | Ile Ala Val Phe Tyr 1665 | Val Ala Glu |
| Gly Gln 1670 | Glu Asp Lys His Ser 1675 | Ile Leu Thr Asn Thr 1680 | Gly Gly Ser |
| Gln Ala | Tyr Glu Asp Phe Val | Ala Gly Leu Gly Trp | Glu Leu Ile |

545

1685

1690

1695

Ile Phe Lys Leu Tyr Glu
1700

<210> 452

<211> 1239

<212> PRT

<213> Homo sapien

<400> 452

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
180 185 190

546

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

547

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp

548

675

680

685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 915 920 925

549

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 995 1000 1005

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe
 1010 1015 1020

Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile
 1025 1030 1035

Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu
 1040 1045 1050

Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala
 1055 1060 1065

Ala Gly Arg Val Ala Ser Ser Ala Phe Leu Asn Ala Pro Arg Val
 1070 1075 1080

Glu Ala Gln Val Leu Leu Gly Ser Leu Val Cys Phe Pro Asn Leu
 1085 1090 1095

Tyr Cys Glu Leu Pro Ser Leu His Pro Asn Ile Pro Asp Val Ala
 1100 1105 1110

Val Ser Gln Phe Thr Asp Val Lys Glu Leu Ile Ile Lys Thr Val
 1115 1120 1125

Leu Ser Ser Ala Arg Asp Glu Pro Ser Gly Pro Ala Arg Cys Val
 1130 1135 1140

Ala Leu Cys Ser Leu Gly Ile Trp Ile Cys Glu Glu Leu Val His
 1145 1150 1155

550

Glu Ser His His Pro Gln Ile Lys Glu Ala Leu Asn Val Ile Cys
 1160 1165 1170

Val Ser Leu Lys Phe Thr Asn Lys Thr Val Ala His Val Ala Cys
 1175 1180 1185

Asn Met Leu His Met Leu Val His Tyr Val Pro Arg Leu Gln Ile
 1190 1195 1200

Tyr Gln Pro Asp Ser Pro Leu Lys Ile Ile Gln Ile Leu Ile Ala
 1205 1210 1215

Thr Ile Thr His Leu Leu Pro Ser Thr Glu Ala Ser Ser Tyr Glu
 1220 1225 1230

Met Asp Lys Arg Val Ile
 1235

<210> 453

<211> 849

<212> PRT

<213> Homo sapien

<400> , 453

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His

551

115

120

125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

552

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

553

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
 675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

Thr Ile Thr Gly Lys Val Ile His Gly Asn Val Phe Leu Lys Cys Ile
 835 840 845

554

Phe

<210> 454
 <211> 284
 <212> PRT
 <213> Homo sapien

<400> 454

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

555

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Val Thr Tyr Leu
 260 265 270

Ser Val Phe Leu Ile Tyr Lys Glu Gly Phe Tyr Leu
 275 280

<210> 455
 <211> 607
 <212> PRT
 <213> Homo sapien

<400> 455

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

556

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile

557

370

375

380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Gly
 595 600 605

<210> 456

<211> 1934

558

<212> PRT

<213> Homo sapien

<400> 456

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

559

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile

560

| | | | | | | |
|---|--|-----|--|-----|--|-----|
| 465 | | 470 | | 475 | | 480 |
| Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu | | | | | | |
| | | 485 | | 490 | | 495 |
| Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu | | | | | | |
| | | 500 | | 505 | | 510 |
| Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu | | | | | | |
| | | 515 | | 520 | | 525 |
| Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln | | | | | | |
| | | 530 | | 535 | | 540 |
| Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys | | | | | | |
| | | 545 | | 550 | | 555 |
| | | | | | | 560 |
| Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro | | | | | | |
| | | 565 | | 570 | | 575 |
| Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro | | | | | | |
| | | 580 | | 585 | | 590 |
| Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Ala Met | | | | | | |
| | | 595 | | 600 | | 605 |
| Arg Ser Arg Ser Ile Gly Glu Cys Ala Leu Pro Ser Ala Tyr Ile Arg | | | | | | |
| | | 610 | | 615 | | 620 |
| Ser Ala Lys Ser Ala Pro Val Leu Ile His Thr Ser Lys Pro Phe Leu | | | | | | |
| | | 625 | | 630 | | 635 |
| | | | | | | 640 |
| Pro Asp Ile Val Leu Thr Pro Leu Ser Asp Glu Leu Ser Asp Ile Asp | | | | | | |
| | | 645 | | 650 | | 655 |
| Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser Gln | | | | | | |
| | | 660 | | 665 | | 670 |
| Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu Gln | | | | | | |
| | | 675 | | 680 | | 685 |
| Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe Thr | | | | | | |
| | | 690 | | 695 | | 700 |
| Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu Pro | | | | | | |
| | | 705 | | 710 | | 715 |
| | | | | | | 720 |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Pro | Leu | Asn | Ser | Asp | Ile | Gly | Gly | Ser | Ser | Ala | Asn | Val | Pro | Asp | Leu | |
| | | | | 725 | | | | | | 730 | | | | | 735 | |
| Met | Asp | Glu | Phe | Ile | Ala | Glu | Arg | Leu | Arg | Ser | Gly | Asn | Ala | Ser | Thr | |
| | | | 740 | | | | | 745 | | | | | 750 | | | |
| Met | Thr | Arg | Arg | Gly | Ser | Ser | Pro | Gly | Ser | Leu | Glu | Ile | Pro | Lys | Asp | |
| | | 755 | | | | | 760 | | | | | 765 | | | | |
| Leu | Pro | Asp | Ile | Leu | Asn | Lys | Gln | Asn | Gln | Met | Arg | Pro | Ile | Asp | Asp | |
| | 770 | | | | | 775 | | | | | 780 | | | | | |
| Pro | Gly | Val | Pro | Ser | Glu | Trp | Thr | Ser | Pro | Ala | Ser | Ala | Gly | Ser | Ser | |
| 785 | | | | | 790 | | | | | 795 | | | | | 800 | |
| Asp | Leu | Ile | Ser | Ser | Asp | Ser | His | Ser | Asp | Ser | Phe | Ser | Ala | Phe | Gln | |
| | | | 805 | | | | | | 810 | | | | | 815 | | |
| Tyr | Asp | Gly | Arg | Lys | Phe | Asp | Asn | Phe | Gly | Phe | Gly | Thr | Asp | Thr | Gly | |
| | | 820 | | | | | | 825 | | | | | 830 | | | |
| Val | Thr | Ser | Ser | Ala | Asp | Val | Asp | Ser | Gly | Ser | Gly | His | His | Gln | Ser | |
| | | 835 | | | | | 840 | | | | | 845 | | | | |
| Ala | Glu | Glu | Gln | Glu | Val | Ala | Ser | Leu | Thr | Thr | Leu | His | Ile | Asp | Ser | |
| | 850 | | | | | 855 | | | | | 860 | | | | | |
| Glu | Thr | Ser | Ser | Leu | Asn | Gln | Gln | Ala | Phe | Ser | Ala | Glu | Val | Ala | Thr | |
| 865 | | | | | 870 | | | | | 875 | | | | | 880 | |
| Ile | Thr | Gly | Ser | Glu | Ser | Ala | Ser | Pro | Val | His | Ser | Pro | Leu | Gly | Ser | |
| | | | 885 | | | | | | 890 | | | | | 895 | | |
| Arg | Ser | Gln | Thr | Pro | Ser | Pro | Ser | Thr | Leu | Asn | Ile | Asp | His | Met | Glu | |
| | | 900 | | | | | | 905 | | | | | 910 | | | |
| Gln | Lys | Asp | Leu | Gln | Leu | Asp | Glu | Lys | Leu | His | His | Ser | Val | Leu | Gln | |
| | | 915 | | | | | 920 | | | | | 925 | | | | |
| Thr | Pro | Asp | Asp | Leu | Glu | Ile | Ser | Glu | Phe | Pro | Ser | Glu | Cys | Cys | Ser | |
| | 930 | | | | | 935 | | | | | 940 | | | | | |
| Val | Met | Ala | Gly | Gly | Thr | Leu | Thr | Gly | Trp | His | Ala | Asp | Val | Ala | Thr | |
| 945 | | | | | 950 | | | | | 955 | | | | | 960 | |

562

Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser Ile
 - 965 970 975

Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu Leu
 980 985 990

Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr Asp
 995 1000 1005

Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 1010 1015 1020

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys
 1025 1030 1035

Tyr Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr
 1040 1045 1050

Met Lys Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr
 1055 1060 1065

His Phe Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln
 1070 1075 1080

Asp Ile Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe
 1085 1090 1095

Ser Leu Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile
 1100 1105 1110

Val Ala Ala Gly Arg Val Ala Ser Ser Ala Phe Leu Asn Ala Pro
 1115 1120 1125

Arg Val Glu Ala Gln Val Leu Leu Gly Ser Leu Val Cys Phe Pro
 1130 1135 1140

Asn Leu Tyr Cys Glu Leu Pro Ser Leu His Pro Asn Ile Pro Asp
 1145 1150 1155

Val Ala Val Ser Gln Phe Thr Asp Val Lys Glu Leu Ile Ile Lys
 1160 1165 1170

Thr Val Leu Ser Ser Ala Arg Asp Glu Pro Ser Gly Pro Ala Arg
 1175 1180 1185

563

| | | | | | |
|---------|-----------------|------|-----------------|------|-------------|
| Cys Val | Ala Leu Cys Ser | Leu | Gly Ile Trp Ile | Cys | Glu Glu Leu |
| 1190 | | 1195 | | 1200 | |
| Val His | Glu Ser His His | Pro | Gln Ile Lys Glu | Ala | Leu Asn Val |
| 1205 | | 1210 | | 1215 | |
| Ile Cys | Val Ser Leu Lys | Phe | Thr Asn Lys Thr | Val | Ala His Val |
| 1220 | | 1225 | | 1230 | |
| Ala Cys | Asn Met Leu His | Met | Leu Val His Tyr | Val | Pro Arg Leu |
| 1235 | | 1240 | | 1245 | |
| Gln Ile | Tyr Gln Pro Asp | Ser | Pro Leu Lys Ile | Ile | Gln Ile Leu |
| 1250 | | 1255 | | 1260 | |
| Ile Ala | Thr Ile Thr His | Leu | Leu Pro Ser Thr | Glu | Ala Ser Ser |
| 1265 | | 1270 | | 1275 | |
| Tyr Glu | Met Asp Lys Arg | Leu | Val Val Ser Leu | Leu | Leu Cys Leu |
| 1280 | | 1285 | | 1290 | |
| Leu Asp | Trp Ile Met Ala | Leu | Pro Leu Lys Thr | Leu | Leu Gln Pro |
| 1295 | | 1300 | | 1305 | |
| Phe His | Ala Thr Gly Ala | Glu | Ser Asp Lys Thr | Glu | Lys Ser Val |
| 1310 | | 1315 | | 1320 | |
| Leu Asn | Cys Ile Tyr Lys | Val | Leu His Gly Cys | Val | Tyr Gly Ala |
| 1325 | | 1330 | | 1335 | |
| Gln Cys | Phe Ser Asn Pro | Arg | Tyr Phe Pro Met | Ser | Leu Ser Asp |
| 1340 | | 1345 | | 1350 | |
| Leu Ala | Ser Val Asp Tyr | Asp | Pro Phe Met His | Leu | Glu Ser Leu |
| 1355 | | 1360 | | 1365 | |
| Lys Glu | Pro Glu Pro Leu | His | Ser Pro Asp Ser | Glu | Arg Ser Ser |
| 1370 | | 1375 | | 1380 | |
| Lys Leu | Gln Pro Val Thr | Glu | Val Lys Thr Gln | Met | Gln His Gly |
| 1385 | | 1390 | | 1395 | |
| Leu Ile | Ser Ile Ala Ala | Arg | Thr Val Ile Thr | His | Leu Val Asn |
| 1400 | | 1405 | | 1410 | |
| His Leu | Gly His Tyr Pro | Met | Ser Gly Gly Pro | Ala | Met Leu Thr |

564

| | | | | |
|---|--|------|--|------|
| 1415 | | 1420 | | 1425 |
| Ser Gln Val Cys Glu Asn His Asp Asn His Tyr Ser Glu Ser Thr | | | | |
| 1430 | | 1435 | | 1440 |
| Glu Leu Ser Pro Glu Leu Phe Glu Ser Pro Asn Ile Gln Phe Phe | | | | |
| 1445 | | 1450 | | 1455 |
| Val Leu Asn Asn Thr Thr Leu Val Ser Cys Ile Gln Ile Arg Ser | | | | |
| 1460 | | 1465 | | 1470 |
| Glu Glu Asn Met Pro Gly Gly Gly Leu Ser Ala Gly Leu Ala Ser | | | | |
| 1475 | | 1480 | | 1485 |
| Ala Asn Ser Asn Val Arg Ile Ile Val Arg Asp Leu Ser Gly Lys | | | | |
| 1490 | | 1495 | | 1500 |
| Tyr Ser Trp Asp Ser Ala Ile Leu Tyr Gly Pro Pro Pro Val Ser | | | | |
| 1505 | | 1510 | | 1515 |
| Gly Leu Ser Glu Pro Thr Ser Phe Met Leu Ser Leu Ser His Gln | | | | |
| 1520 | | 1525 | | 1530 |
| Glu Lys Pro Glu Glu Pro Pro Thr Ser Asn Glu Cys Leu Glu Asp | | | | |
| 1535 | | 1540 | | 1545 |
| Ile Thr Val Lys Asp Gly Leu Ser Leu Gln Phe Lys Arg Phe Arg | | | | |
| 1550 | | 1555 | | 1560 |
| Glu Thr Val Pro Thr Trp Asp Thr Ile Arg Asp Glu Glu Asp Val | | | | |
| 1565 | | 1570 | | 1575 |
| Leu Asp Glu Leu Leu Gln Tyr Leu Gly Val Thr Ser Pro Glu Cys | | | | |
| 1580 | | 1585 | | 1590 |
| Leu Gln Arg Thr Gly Ile Ser Leu Asn Ile Pro Ala Pro Gln Pro | | | | |
| 1595 | | 1600 | | 1605 |
| Val Cys Ile Ser Glu Lys Gln Glu Asn Asp Val Ile Asn Ala Ile | | | | |
| 1610 | | 1615 | | 1620 |
| Leu Lys Gln His Thr Glu Glu Lys Glu Phe Val Glu Lys His Phe | | | | |
| 1625 | | 1630 | | 1635 |
| Asn Asp Leu Asn Met Lys Ala Val Glu Gln Asp Glu Pro Ile Pro | | | | |
| 1640 | | 1645 | | 1650 |

565

| | | | | |
|---------|---------------------|-----------------|---------------------|-----------------|
| Gln Lys | Pro Gln Ser Ala Phe | Tyr Tyr Cys Arg | Leu | Leu Leu Ser |
| 1655 | | 1660 | 1665 | |
| Ile Leu | Gly Met Asn Ser Trp | Asp Lys Arg Arg | Ser | Phe His Leu |
| 1670 | | 1675 | 1680 | |
| Leu Lys | Lys Asn Glu Lys | Leu | Leu Arg Glu Leu Arg | Asn Leu Asp |
| 1685 | | 1690 | 1695 | |
| Ser Arg | Gln Cys Arg Glu Thr | His Lys Ile Ala | Val | Phe Tyr Val |
| 1700 | | 1705 | 1710 | |
| Ala Glu | Gly Gln Glu Asp | Lys | His Ser Ile Leu Thr | Asn Thr Gly |
| 1715 | | 1720 | 1725 | |
| Gly Ser | Gln Ala Tyr Glu | Asp | Phe Val Ala Gly | Leu Gly Trp Glu |
| 1730 | | 1735 | 1740 | |
| Val Asn | Leu Thr Asn His | Cys | Gly Phe Met Gly Gly | Leu Gln Lys |
| 1745 | | 1750 | 1755 | |
| Asn Lys | Ser Thr Gly Leu | Thr | Thr Pro Tyr Phe | Ala Thr Ser Thr |
| 1760 | | 1765 | 1770 | |
| Val Glu | Val Ile Phe His | Val | Ser Thr Arg Met | Pro Ser Asp Ser |
| 1775 | | 1780 | 1785 | |
| Asp Asp | Ser Leu Thr Lys | Lys | Leu Arg His Leu | Gly Asn Asp Glu |
| 1790 | | 1795 | 1800 | |
| Val His | Ile Val Trp Ser | Glu | His Thr Arg Asp | Tyr Arg Arg Gly |
| 1805 | | 1810 | 1815 | |
| Ile Ile | Pro Thr Glu Phe | Gly | Asp Val Leu Ile | Val Ile Tyr Pro |
| 1820 | | 1825 | 1830 | |
| Met Lys | Asn His Met Phe | Ser | Ile Gln Ile Met | Lys Lys Pro Glu |
| 1835 | | 1840 | 1845 | |
| Val Pro | Phe Phe Gly Pro | Leu | Phe Asp Gly Ala | Ile Val Asn Gly |
| 1850 | | 1855 | 1860 | |
| Lys Val | Leu Pro Ile Met | Val | Arg Ala Thr Ala | Ile Asn Ala Ser |
| 1865 | | 1870 | 1875 | |

566

Arg Ala Leu Lys Ser Leu Ile Pro Leu Tyr Gln Asn Phe Tyr Glu
 1880 1885 1890

Glu Arg Ala Arg Tyr Leu Gln Thr Ile Val Gln His His Leu Glu
 1895 1900 1905

Pro Thr Thr Phe Glu Asp Phe Ala Ala Gln Val Phe Ser Pro Ala
 1910 1915 1920

Pro Tyr His His Leu Pro Ser Asp Ala Asp His
 1925 1930

<210> 457

<211> 1220

<212> PRT

<213> Homo sapien

<400> 457

Met Ser Gln Lys Leu Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser
 1 5 10 15

Ala Asn Val Pro Asp Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg
 20 25 30

Ser Gly Asn Ala Ser Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser
 35 40 45

Leu Glu Ile Pro Lys Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln
 50 55 60

Met Arg Pro Ile Asp Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro
 65 70 75 80

Ala Ser Ala Gly Ser Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp
 85 90 95

Ser Phe Ser Ala Phe Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly
 100 105 110

Phe Gly Thr Asp Thr Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly
 115 120 125

Ser Gly His His Gln Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr
 130 135 140

Thr Leu His Ile Asp Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe

567

| | | | | | | |
|---|---|-----------------------------|-----|-----|-----|-----|
| 145 | | 150 | | 155 | | 160 |
| Ser Ala Glu Val | Ala Thr Ile Thr Gly | Ser Glu Ser Ala Ser Pro Val | | | | |
| | 165 | 170 | | | 175 | |
| His Ser Pro Leu Gly | Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu | | | | | |
| | 180 | 185 | | | 190 | |
| Asn Ile Asp His Met Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu | | | | | | |
| | 195 | 200 | | | 205 | |
| His His Ser Val Leu Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe | | | | | | |
| | 210 | 215 | | | 220 | |
| Pro Ser Glu Cys Cys Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp | | | | | | |
| | 225 | 230 | | | 235 | 240 |
| His Ala Asp Val Ala Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu | | | | | | |
| | 245 | | 250 | | | 255 |
| Gly Asp Val Asn Ser Ile Met Asp Pro Glu Ile His Ala Gln Val Phe | | | | | | |
| | 260 | | 265 | | | 270 |
| Asp Tyr Leu Cys Glu Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn | | | | | | |
| | 275 | | 280 | | | 285 |
| Leu Gly Ile Ser Thr Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu | | | | | | |
| | 290 | | 295 | | | 300 |
| Ile Pro Pro Leu Arg Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met | | | | | | |
| | 305 | | 310 | | | 315 |
| Leu Thr Asp Lys Tyr Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile | | | | | | |
| | 325 | | | | 330 | 335 |
| Cys Asn Thr Met Lys Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe | | | | | | |
| | 340 | | | | 345 | 350 |
| Leu Thr His Phe Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp | | | | | | |
| | 355 | | | | 360 | 365 |
| Gln Asp Ile Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe | | | | | | |
| | 370 | | | | 375 | 380 |
| Ser Leu Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val | | | | | | |
| | 385 | | | | 390 | 395 |
| | | | | | | 400 |

568

Ala Ala Gly Arg Val Ala Ser Ser Ala Phe Leu Asn Ala Pro Arg Val
 405 410 415

Glu Ala Gln Val Leu Leu Gly Ser Leu Val Cys Phe Pro Asn Leu Tyr
 420 425 430

Cys Glu Leu Pro Ser Leu His Pro Asn Ile Pro Asp Val Ala Val Ser
 435 440 445

Gln Phe Thr Asp Val Lys Glu Leu Ile Ile Lys Thr Val Leu Ser Ser
 450 455 460

Ala Arg Asp Glu Pro Ser Gly Pro Ala Arg Cys Val Ala Leu Cys Ser
 465 470 475 480

Leu Gly Ile Trp Ile Cys Glu Glu Leu Val His Glu Ser His His Pro
 485 490 495

Gln Ile Lys Glu Ala Leu Asn Val Ile Cys Val Ser Leu Lys Phe Thr
 500 505 510

Asn Lys Thr Val Ala His Val Ala Cys Asn Met Leu His Met Leu Val
 515 520 525

His Tyr Val Pro Arg Leu Gln Ile Tyr Gln Pro Asp Ser Pro Leu Lys
 530 535 540

Ile Ile Gln Ile Leu Ile Ala Thr Ile Thr His Leu Leu Pro Ser Thr
 545 550 555 560

Glu Ala Ser Ser Tyr Glu Met Asp Lys Arg Leu Val Val Ser Leu Leu
 565 570 575

Leu Cys Leu Leu Asp Trp Ile Met Ala Leu Pro Leu Lys Thr Leu Leu
 580 585 590

Gln Pro Phe His Ala Thr Gly Ala Glu Ser Asp Lys Thr Glu Lys Ser
 595 600 605

Val Leu Asn Cys Ile Tyr Lys Val Leu His Gly Cys Val Tyr Gly Ala
 610 615 620

Gln Cys Phe Ser Asn Pro Arg Tyr Phe Pro Met Ser Leu Ser Asp Leu
 625 630 635 640

569

Ala Ser Val Asp Tyr Asp Pro Phe Met His Leu Glu Ser Leu Lys Glu
 645 650 655

Pro Glu Pro Leu His Ser Pro Asp Ser Glu Arg Ser Ser Lys Leu Gln
 660 665 670

Pro Val Thr Glu Val Lys Thr Gln Met Gln His Gly Leu Ile Ser Ile
 675 680 685

Ala Ala Arg Thr Val Ile Thr His Leu Val Asn His Leu Gly His Tyr
 690 695 700

Pro Met Ser Gly Gly Pro Ala Met Leu Thr Ser Gln Val Cys Glu Asn
 705 710 715 720

His Asp Asn His Tyr Ser Glu Ser Thr Glu Leu Ser Pro Glu Leu Phe
 725 730 735

Glu Ser Pro Asn Ile Gln Phe Phe Val Leu Asn Asn Thr Thr Leu Val
 740 745 750

Ser Cys Ile Gln Ile Arg Ser Glu Glu Asn Met Pro Gly Gly Gly Leu
 755 760 765

Ser Ala Gly Leu Ala Ser Ala Asn Ser Asn Val Arg Ile Ile Val Arg
 770 775 780

Asp Leu Ser Gly Lys Tyr Ser Trp Asp Ser Ala Ile Leu Tyr Gly Pro
 785 790 795 800

Pro Pro Val Ser Gly Leu Ser Glu Pro Thr Ser Phe Met Leu Ser Leu
 805 810 815

Ser His Gln Glu Lys Pro Glu Glu Pro Pro Thr Ser Asn Glu Cys Leu
 820 825 830

Glu Asp Ile Thr Val Lys Asp Gly Leu Ser Leu Gln Phe Lys Arg Phe
 835 840 845

Arg Glu Thr Val Pro Thr Trp Asp Thr Ile Arg Asp Glu Glu Asp Val
 850 855 860

Leu Asp Glu Leu Leu Gln Tyr Leu Gly Val Thr Ser Pro Glu Cys Leu
 865 870 875 880

570

Gln Arg Thr Gly Ile Ser Leu Asn Ile Pro Ala Pro Gln Pro Val Cys
 885 890 895

Ile Ser Glu Lys Gln Glu Asn Asp Val Ile Asn Ala Ile Leu Lys Gln
 900 905 910

His Thr Glu Glu Lys Glu Phe Val Glu Lys His Phe Asn Asp Leu Asn
 915 920 925

Met Lys Ala Val Glu Gln Asp Glu Pro Ile Pro Gln Lys Pro Gln Ser
 930 935 940

Ala Phe Tyr Tyr Cys Arg Leu Leu Leu Ser Ile Leu Gly Met Asn Ser
 945 950 955 960

Trp Asp Lys Arg Arg Ser Phe His Leu Leu Lys Lys Asn Glu Lys Leu
 965 970 975

Leu Arg Glu Leu Arg Asn Leu Asp Ser Arg Gln Cys Arg Glu Thr His
 980 985 990

Lys Ile Ala Val Phe Tyr Val Ala Glu Gly Gln Glu Asp Lys His Ser
 995 1000 1005

Ile Leu Thr Asn Thr Gly Gly Ser Gln Ala Tyr Glu Asp Phe Val
 1010 1015 1020

Ala Gly Leu Gly Trp Glu Val Asn Leu Thr Asn His Cys Gly Phe
 1025 1030 1035

Met Gly Gly Leu Gln Lys Asn Lys Ser Thr Gly Leu Thr Thr Pro
 1040 1045 1050

Tyr Phe Ala Thr Ser Thr Val Glu Val Ile Phe His Val Ser Thr
 1055 1060 1065

Arg Met Pro Ser Asp Ser Asp Asp Ser Leu Thr Lys Lys Leu Arg
 1070 1075 1080

His Leu Gly Asn Asp Glu Val His Ile Val Trp Ser Glu His Thr
 1085 1090 1095

Arg Asp Tyr Arg Arg Gly Ile Ile Pro Thr Glu Phe Gly Asp Val
 1100 1105 1110

Leu Ile Val Ile Tyr Pro Met Lys Asn His Met Phe Ser Ile Gln

571

1115

1120

1125

Ile Met Lys Lys Pro Glu Val Pro Phe Phe Gly Pro Leu Phe Asp
 1130 1135 1140

Gly Ala Ile Val Asn Gly Lys Val Leu Pro Ile Met Val Arg Ala
 1145 1150 1155

Thr Ala Ile Asn Ala Ser Arg Ala Leu Lys Ser Leu Ile Pro Leu
 1160 1165 1170

Tyr Gln Asn Phe Tyr Glu Glu Arg Ala Arg Tyr Leu Gln Thr Ile
 1175 1180 1185

Val Gln His His Leu Glu Pro Thr Thr Phe Glu Asp Phe Ala Ala
 1190 1195 1200

Gln Val Phe Ser Pro Ala Pro Tyr His His Leu Pro Ser Asp Ala
 1205 1210 1215

Asp His
 1220

<210> 458
 <211> 1126
 <212> PRT
 <213> Homo sapien

<400> 458

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

572

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

573

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro

574

580

585

590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
 675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

575

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 915 920 925

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 995 1000 1005

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe
 1010 1015 1020

Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile
 1025 1030 1035

Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu
 1040 1045 1050

Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala
 1055 1060 1065

576

Ala Gly Arg Val Ala Ser Ser Ala Phe Leu Asn Ala Pro Arg Val
 1070 1075 1080

Glu Ala Gln Val Leu Leu Gly Ser Leu Val Cys Phe Pro Asn Leu
 1085 1090 1095

Tyr Cys Glu Leu Pro Ser Leu His Pro Asn Ile Pro Asp Val Ala
 1100 1105 1110

Val Ser Gln Phe Thr Asp Val Lys Met Cys Ser Thr Leu
 1115 1120 1125

<210> 459

<211> 1894

<212> PRT

<213> Homo sapien

<400> 459

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu

577

| | | | | | | |
|-----------------|-----------------|-------------|-------------|-------------|-----|-----|
| 145 | | 150 | | 155 | | 160 |
| Val Ser Phe Trp | Leu Glu Pro Lys | Pro His Thr | Gly Pro His | Ile Pro | | |
| | 165 | | 170 | | 175 | |
| Gly Met Glu Gly | Glu Val Leu Pro | Lys Asn Ile | Gln Arg Ala | Ala Ala Ala | | |
| | 180 | | 185 | | 190 | |
| Ser Leu Val Ser | Arg Glu Glu Ser | Lys Asn Asp | Asn Ala Asp | Lys Thr | | |
| | 195 | | 200 | | 205 | |
| Asp Arg Thr Thr | Glu Pro Glu Gln | Ser His Ser | Asn Thr Ser | Thr Leu | | |
| | 210 | | 215 | | 220 | |
| Thr Glu Arg Glu | Pro Ser Ser Ser | Ser Leu Cys | Ser Ile Asp | Glu Glu | | |
| | 225 | | 230 | | 235 | |
| His Leu Thr Asp | Ile Glu Ile Val | Arg Arg Val | Phe Ser Ser | Lys Arg | | |
| | 245 | | 250 | | 255 | |
| Ser Asn Val Asn | Phe Val Thr Glu | Ile Phe Arg | Gln Ala Phe | Leu Leu | | |
| | 260 | | 265 | | 270 | |
| Pro Ile Cys Glu | Ala Ala Ala Met | Arg Lys Val | Val Lys Val | Tyr Gln | | |
| | 275 | | 280 | | 285 | |
| Glu Trp Ile Gln | Gln Glu Glu Lys | Pro Leu Phe | Met Gln Glu | Pro Glu | | |
| | 290 | | 295 | | 300 | |
| Glu Ile Val Ile | Thr Ser Ser Asp | Leu Pro Cys | Ile Glu Asn | Val Thr | | |
| | 305 | | 310 | | 315 | |
| Asp His Asp Ile | Ser Met Glu Glu | Gly Glu Lys | Arg Glu Glu | Glu Asn | | |
| | 325 | | 330 | | 335 | |
| Gly Thr Asn Thr | Ala Asp His Val | Arg Asn Ser | Ser Trp Ala | Lys Asn | | |
| | 340 | | 345 | | 350 | |
| Gly Ser Tyr Gln | Gly Ala Leu His | Asn Ala Ser | Glu Glu Ala | Thr Glu | | |
| | 355 | | 360 | | 365 | |
| Gln Asn Ile Arg | Ala Gly Thr Gln | Ala Val Leu | Gln Val Phe | Ile Ile | | |
| | 370 | | 375 | | 380 | |
| Asn Ser Ser Asn | Ile Phe Leu Leu | Glu Pro Ala | Asn Glu Ile | Lys Asn | | |
| | 385 | | 390 | | 395 | |
| | | | | | 400 | |

578

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Gln | Pro | Leu | Pro | Arg | Ser | Ser | Ser | Thr | Ser | Asp | Ile | Leu | Glu | Pro | Phe | |
| | | | | 645 | | | | | 650 | | | | | 655 | | |
| Thr | Val | Glu | Arg | Ala | Lys | Val | Asn | Lys | Glu | Asp | Met | Ser | Gln | Lys | Leu | |
| | | | | 660 | | | | | 665 | | | | | 670 | | |
| Pro | Pro | Leu | Asn | Ser | Asp | Ile | Gly | Gly | Ser | Ser | Ala | Asn | Val | Pro | Asp | |
| | | | | 675 | | | | | 680 | | | | | 685 | | |
| Leu | Met | Asp | Glu | Phe | Ile | Ala | Glu | Arg | Leu | Arg | Ser | Gly | Asn | Ala | Ser | |
| | | | | 690 | | | | | 695 | | | | | 700 | | |
| Thr | Met | Thr | Arg | Arg | Gly | Ser | Ser | Pro | Gly | Ser | Leu | Glu | Ile | Pro | Lys | |
| | | | | 705 | | | | | 710 | | | | | 715 | | |
| Asp | Leu | Pro | Asp | Ile | Leu | Asn | Lys | Gln | Asn | Gln | Met | Arg | Pro | Ile | Asp | |
| | | | | 725 | | | | | 730 | | | | | 735 | | |
| Asp | Pro | Gly | Val | Pro | Ser | Glu | Trp | Thr | Ser | Pro | Ala | Ser | Ala | Gly | Ser | |
| | | | | 740 | | | | | 745 | | | | | 750 | | |
| Ser | Asp | Leu | Ile | Ser | Ser | Asp | Ser | His | Ser | Asp | Ser | Phe | Ser | Ala | Phe | |
| | | | | 755 | | | | | 760 | | | | | 765 | | |
| Gln | Tyr | Asp | Gly | Arg | Lys | Phe | Asp | Asn | Phe | Gly | Phe | Gly | Thr | Asp | Thr | |
| | | | | 770 | | | | | 775 | | | | | 780 | | |
| Gly | Val | Thr | Ser | Ser | Ala | Asp | Val | Asp | Ser | Gly | Ser | Gly | His | His | Gln | |
| | | | | 785 | | | | | 790 | | | | | 795 | | |
| Ser | Ala | Glu | Glu | Gln | Glu | Val | Ala | Ser | Leu | Thr | Thr | Leu | His | Ile | Asp | |
| | | | | 805 | | | | | 810 | | | | | 815 | | |
| Ser | Glu | Thr | Ser | Ser | Leu | Asn | Gln | Gln | Ala | Phe | Ser | Ala | Glu | Val | Ala | |
| | | | | 820 | | | | | 825 | | | | | 830 | | |
| Thr | Ile | Thr | Gly | Ser | Glu | Ser | Ala | Ser | Pro | Val | His | Ser | Pro | Leu | Gly | |
| | | | | 835 | | | | | 840 | | | | | 845 | | |
| Ser | Arg | Ser | Gln | Thr | Pro | Ser | Pro | Ser | Thr | Leu | Asn | Ile | Asp | His | Met | |
| | | | | 850 | | | | | 855 | | | | | 860 | | |
| Glu | Gln | Lys | Asp | Leu | Gln | Leu | Asp | Glu | Lys | Leu | His | His | Ser | Val | Leu | |
| | | | | 865 | | | | | 870 | | | | | 875 | | |

| Gln | Thr | Pro | Asp | Asp | Leu | Glu | Ile | Ser | Glu | Phe | Pro | Ser | Glu | Cys | Cys | |
|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|--|
| | | | | 885 | | | | | 890 | | | | | | | |
| Ser | Val | Met | Ala | Gly | Gly | Thr | Leu | Thr | Gly | Trp | His | Ala | Asp | Val | Ala | |
| | | | 900 | | | | | 905 | | | | | | | | |
| Thr | Val | Met | Trp | Arg | Arg | Met | Leu | Gly | Ile | Leu | Gly | Asp | Val | Asn | Ser | |
| | | | 915 | | | | | 920 | | | | | | | | |
| Ile | Met | Asp | Pro | Glu | Ile | His | Ala | Gln | Val | Phe | Asp | Tyr | Leu | Cys | Glu | |
| | | | 930 | | | | | 935 | | | | | | | | |
| Leu | Trp | Gln | Asn | Leu | Ala | Lys | Ile | Arg | Asp | Asn | Leu | Gly | Ile | Ser | Thr | |
| 945 | | | | | 950 | | | | | 955 | | | | | | |
| Asp | Asn | Leu | Thr | Ser | Pro | Ser | Pro | Pro | Val | Leu | Ile | Pro | Pro | Leu | Arg | |
| | | | 965 | | | | | 970 | | | | | | | | |
| Ile | Leu | Thr | Pro | Trp | Leu | Phe | Lys | Ala | Thr | Met | Leu | Thr | Asp | Lys | Tyr | |
| | | | 980 | | | | | 985 | | | | | | | | |
| Lys | Gln | Gly | Lys | Leu | His | Ala | Tyr | Lys | Leu | Ile | Cys | Asn | Thr | Met | Lys | |
| | | | 995 | | | | | 1000 | | | | | | | | |
| Arg | Arg | Gln | Asp | Val | Ser | Pro | Asn | Arg | Asp | Phe | Leu | Thr | His | Phe | | |
| | | | 1010 | | | | | 1015 | | | | | | | | |
| Tyr | Asn | Ile | Met | His | Cys | Gly | Leu | Leu | His | Ile | Asp | Gln | Asp | Ile | | |
| | | | 1025 | | | | | 1030 | | | | | | | | |
| Val | Asn | Thr | Ile | Ile | Lys | His | Cys | Ser | Pro | Gln | Phe | Phe | Ser | Leu | | |
| | | | 1040 | | | | | 1045 | | | | | | | | |
| Gly | Leu | Pro | Gly | Ala | Thr | Met | Leu | Ile | Met | Asp | Phe | Ile | Val | Ala | | |
| | | | 1055 | | | | | 1060 | | | | | | | | |
| Ala | Gly | Arg | Val | Ala | Ser | Ser | Ala | Phe | Leu | Asn | Ala | Pro | Arg | Val | | |
| | | | 1070 | | | | | 1075 | | | | | | | | |
| Glu | Ala | Gln | Val | Leu | Leu | Gly | Ser | Leu | Val | Cys | Phe | Pro | Asn | Leu | | |
| | | | 1085 | | | | | 1090 | | | | | | | | |
| Tyr | Cys | Glu | Leu | Pro | Ser | Leu | His | Pro | Asn | Ile | Pro | Asp | Val | Ala | | |
| | | | 1100 | | | | | 1105 | | | | | | | | |
| Val | Ser | Gln | Phe | Thr | Asp | Val | Lys | Glu | Leu | Ile | Ile | Lys | Thr | Val | | |

581

| | | |
|---|------|------|
| 1115 | 1120 | 1125 |
| Leu Ser Ser Ala Arg Asp Glu Pro Ser Gly Pro Ala Arg Cys Val | | |
| 1130 | 1135 | 1140 |
| Ala Leu Cys Ser Leu Gly Ile Trp Ile Cys Glu Glu Leu Val His | | |
| 1145 | 1150 | 1155 |
| Glu Ser His His Pro Gln Ile Lys Glu Ala Leu Asn Val Ile Cys | | |
| 1160 | 1165 | 1170 |
| Val Ser Leu Lys Phe Thr Asn Lys Thr Val Ala His Val Ala Cys | | |
| 1175 | 1180 | 1185 |
| Asn Met Leu His Met Leu Val His Tyr Val Pro Arg Leu Gln Ile | | |
| 1190 | 1195 | 1200 |
| Tyr Gln Pro Asp Ser Pro Leu Lys Ile Ile Gln Ile Leu Ile Ala | | |
| 1205 | 1210 | 1215 |
| Thr Ile Thr His Leu Leu Pro Ser Thr Glu Ala Ser Ser Tyr Glu | | |
| 1220 | 1225 | 1230 |
| Met Asp Lys Arg Leu Val Val Ser Leu Leu Leu Cys Leu Leu Asp | | |
| 1235 | 1240 | 1245 |
| Trp Ile Met Ala Leu Pro Leu Lys Thr Leu Leu Gln Pro Phe His | | |
| 1250 | 1255 | 1260 |
| Ala Thr Gly Ala Glu Ser Asp Lys Thr Glu Lys Ser Val Leu Asn | | |
| 1265 | 1270 | 1275 |
| Cys Ile Tyr Lys Val Leu His Gly Cys Val Tyr Gly Ala Gln Cys | | |
| 1280 | 1285 | 1290 |
| Phe Ser Asn Pro Arg Tyr Phe Pro Met Ser Leu Ser Asp Leu Ala | | |
| 1295 | 1300 | 1305 |
| Ser Val Asp Tyr Asp Pro Phe Met His Leu Glu Ser Leu Lys Glu | | |
| 1310 | 1315 | 1320 |
| Pro Glu Pro Leu His Ser Pro Asp Ser Glu Arg Ser Ser Lys Leu | | |
| 1325 | 1330 | 1335 |
| Gln Pro Val Thr Glu Val Lys Thr Gln Met Gln His Gly Leu Ile | | |
| 1340 | 1345 | 1350 |

583

| | | |
|-----------------------------|---------------------|-------------|
| Gln His Thr Glu Glu Lys Glu | Phe Val Glu Lys His | Phe Asn Asp |
| 1580 | 1585 | 1590 |
| Leu Asn Met Lys Ala Val Glu | Gln Asp Glu Pro Ile | Pro Gln Lys |
| 1595 | 1600 | 1605 |
| Pro Gln Ser Ala Phe Tyr Tyr | Cys Arg Leu Leu Leu | Ser Ile Leu |
| 1610 | 1615 | 1620 |
| Gly Met Asn Ser Trp Asp Lys | Arg Arg Ser Phe His | Leu Leu Lys |
| 1625 | 1630 | 1635 |
| Lys Asn Glu Lys Leu Leu Arg | Glu Leu Arg Asn Leu | Asp Ser Arg |
| 1640 | 1645 | 1650 |
| Gln Cys Arg Glu Thr His Lys | Ile Ala Val Phe Tyr | Val Ala Glu |
| 1655 | 1660 | 1665 |
| Gly Gln Glu Asp Lys His Ser | Ile Leu Thr Asn Thr | Gly Gly Ser |
| 1670 | 1675 | 1680 |
| Gln Ala Tyr Glu Asp Phe Val | Ala Gly Leu Gly Trp | Glu Val Asn |
| 1685 | 1690 | 1695 |
| Leu Thr Asn His Cys Gly Phe | Met Gly Gly Leu Gln | Lys Asn Lys |
| 1700 | 1705 | 1710 |
| Ser Thr Gly Leu Thr Thr Pro | Tyr Phe Ala Thr Ser | Thr Val Glu |
| 1715 | 1720 | 1725 |
| Val Ile Phe His Val Ser Thr | Arg Met Pro Ser Asp | Ser Asp Asp |
| 1730 | 1735 | 1740 |
| Ser Leu Thr Lys Lys Leu Arg | His Leu Gly Asn Asp | Glu Val His |
| 1745 | 1750 | 1755 |
| Ile Val Trp Ser Glu His Thr | Arg Asp Tyr Arg Arg | Gly Ile Ile |
| 1760 | 1765 | 1770 |
| Pro Thr Glu Phe Gly Asp Val | Leu Ile Val Ile Tyr | Pro Met Lys |
| 1775 | 1780 | 1785 |
| Asn His Met Phe Ser Ile Gln | Ile Met Lys Lys Pro | Glu Val Pro |
| 1790 | 1795 | 1800 |

584

Phe Phe Gly Pro Leu Phe Asp Gly Ala Ile Val Asn Gly Lys Val
 1805 1810 1815

Leu Pro Ile Met Val Arg Ala Thr Ala Ile Asn Ala Ser Arg Ala
 1820 1825 1830

Leu Lys Ser Leu Ile Pro Leu Tyr Gln Asn Phe Tyr Glu Glu Arg
 1835 1840 1845

Ala Arg Tyr Leu Gln Thr Ile Val Gln His His Leu Glu Pro Thr
 1850 1855 1860

Thr Phe Glu Asp Phe Ala Ala Gln Val Phe Ser Pro Ala Pro Tyr
 1865 1870 1875

His His Leu Pro Ser Asp Ala Gly Leu Leu Pro Arg Asp Ser Thr
 1880 1885 1890

Gln

<210> 460
 <211> 1867
 <212> PRT
 <213> Homo sapien

<400> 460

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

585

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

586

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

587

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
820 825 830

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly

588

| | | |
|---|------|-----------|
| 835 | 840 | 845 |
| Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met | | |
| 850 | 855 | 860 |
| Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu | | |
| 865 | 870 | 875 880 |
| Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys | | |
| | 885 | 890 895 |
| Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala | | |
| | 900 | 905 910 |
| Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser | | |
| | 915 | 920 925 |
| Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu | | |
| | 930 | 935 940 |
| Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr | | |
| 945 | 950 | 955 960 |
| Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg | | |
| | 965 | 970 975 |
| Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr | | |
| | 980 | 985 990 |
| Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys | | |
| | 995 | 1000 1005 |
| Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe | | |
| 1010 | 1015 | 1020 |
| Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile | | |
| 1025 | 1030 | 1035 |
| Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu | | |
| 1040 | 1045 | 1050 |
| Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala | | |
| 1055 | 1060 | 1065 |
| Ala Gly Arg Val Ala Ser Ser Ala Phe Leu Asn Ala Pro Arg Val | | |
| 1070 | 1075 | 1080 |

589

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Glu | Ala | Gln | Val | Leu | Leu | Gly | Ser | Leu | Val | Cys | Phe | Pro | Asn | Leu |
| 1085 | | | | | | 1090 | | | | | 1095 | | | |
| Tyr | Cys | Glu | Leu | Pro | Ser | Leu | His | Pro | Asn | Ile | Pro | Asp | Val | Ala |
| 1100 | | | | | | 1105 | | | | | 1110 | | | |
| Val | Ser | Gln | Phe | Thr | Asp | Val | Lys | Glu | Leu | Ile | Ile | Lys | Thr | Val |
| 1115 | | | | | | 1120 | | | | | 1125 | | | |
| Leu | Ser | Ser | Ala | Arg | Asp | Glu | Pro | Ser | Gly | Pro | Ala | Arg | Cys | Val |
| 1130 | | | | | | 1135 | | | | | 1140 | | | |
| Ala | Leu | Cys | Ser | Leu | Gly | Ile | Trp | Ile | Cys | Glu | Glu | Leu | Val | His |
| 1145 | | | | | | 1150 | | | | | 1155 | | | |
| Glu | Ser | His | His | Pro | Gln | Ile | Lys | Glu | Ala | Leu | Asn | Val | Ile | Cys |
| 1160 | | | | | | 1165 | | | | | 1170 | | | |
| Val | Ser | Leu | Lys | Phe | Thr | Asn | Lys | Thr | Val | Ala | His | Val | Ala | Cys |
| 1175 | | | | | | 1180 | | | | | 1185 | | | |
| Asn | Met | Leu | His | Met | Leu | Val | His | Tyr | Val | Pro | Arg | Leu | Gln | Ile |
| 1190 | | | | | | 1195 | | | | | 1200 | | | |
| Tyr | Gln | Pro | Asp | Ser | Pro | Leu | Lys | Ile | Ile | Gln | Ile | Leu | Ile | Ala |
| 1205 | | | | | | 1210 | | | | | 1215 | | | |
| Thr | Ile | Thr | His | Leu | Leu | Pro | Ser | Thr | Glu | Ala | Ser | Ser | Tyr | Glu |
| 1220 | | | | | | 1225 | | | | | 1230 | | | |
| Met | Asp | Lys | Arg | Leu | Val | Val | Ser | Leu | Leu | Leu | Cys | Leu | Leu | Asp |
| 1235 | | | | | | 1240 | | | | | 1245 | | | |
| Trp | Ile | Met | Ala | Leu | Pro | Leu | Lys | Thr | Leu | Leu | Gln | Pro | Phe | His |
| 1250 | | | | | | 1255 | | | | | 1260 | | | |
| Ala | Thr | Gly | Ala | Glu | Ser | Asp | Lys | Thr | Glu | Lys | Ser | Val | Leu | Asn |
| 1265 | | | | | | 1270 | | | | | 1275 | | | |
| Cys | Ile | Tyr | Lys | Val | Leu | His | Gly | Cys | Val | Tyr | Gly | Ala | Gln | Cys |
| 1280 | | | | | | 1285 | | | | | 1290 | | | |
| Phe | Ser | Asn | Pro | Arg | Tyr | Phe | Pro | Met | Ser | Leu | Ser | Asp | Leu | Ala |
| 1295 | | | | | | 1300 | | | | | 1305 | | | |

590

| | | | | | | | |
|---------|---------|---------|---------|---------|---------|---------|-----|
| Ser Val | Asp Tyr | Asp Pro | Phe Met | His Leu | Glu Ser | Leu Lys | Glu |
| 1310 | | | 1315 | | 1320 | | |
| Pro Glu | Pro Leu | His Ser | Pro Asp | Ser Glu | Arg Ser | Ser Lys | Leu |
| 1325 | | | 1330 | | 1335 | | |
| Gln Pro | Val Thr | Glu Val | Lys Thr | Gln Met | Gln His | Gly Leu | Ile |
| 1340 | | | 1345 | | 1350 | | |
| Ser Ile | Ala Ala | Arg Thr | Val Ile | Thr His | Leu Val | Asn His | Leu |
| 1355 | | | 1360 | | 1365 | | |
| Gly His | Tyr Pro | Met Ser | Gly Gly | Pro Ala | Met Leu | Thr Ser | Gln |
| 1370 | | | 1375 | | 1380 | | |
| Val Cys | Glu Asn | His Asp | Asn His | Tyr Ser | Glu Ser | Thr Glu | Leu |
| 1385 | | | 1390 | | 1395 | | |
| Ser Pro | Glu Leu | Phe Glu | Ser Pro | Asn Ile | Gln Phe | Phe Val | Leu |
| 1400 | | | 1405 | | 1410 | | |
| Asn Asn | Thr Thr | Leu Val | Ser Cys | Ile Gln | Ile Arg | Ser Glu | Glu |
| 1415 | | | 1420 | | 1425 | | |
| Asn Met | Pro Gly | Gly Gly | Leu Ser | Ala Gly | Leu Ala | Ser Ala | Asn |
| 1430 | | | 1435 | | 1440 | | |
| Ser Asn | Val Arg | Ile Ile | Val Arg | Asp Leu | Ser Gly | Lys Tyr | Ser |
| 1445 | | | 1450 | | 1455 | | |
| Trp Asp | Ser Ala | Ile Leu | Tyr Gly | Pro Pro | Pro Val | Ser Gly | Leu |
| 1460 | | | 1465 | | 1470 | | |
| Ser Glu | Pro Thr | Ser Phe | Met Leu | Ser Leu | Ser His | Gln Glu | Lys |
| 1475 | | | 1480 | | 1485 | | |
| Pro Glu | Glu Pro | Pro Thr | Ser Asn | Glu Cys | Leu Glu | Asp Ile | Thr |
| 1490 | | | 1495 | | 1500 | | |
| Val Lys | Asp Gly | Leu Ser | Leu Gln | Phe Lys | Arg Phe | Arg Glu | Thr |
| 1505 | | | 1510 | | 1515 | | |
| Val Pro | Thr Trp | Asp Thr | Ile Arg | Asp Glu | Glu Asp | Val Leu | Asp |
| 1520 | | | 1525 | | 1530 | | |

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| | | | |
|---------|---------------------|---------------------|-------------|
| Glu Leu | Leu Gln Tyr Leu Gly | Val Thr Ser Pro Glu | Cys Leu Gln |
| 1535 | 1540 | 1545 | |
| Arg Thr | Gly Ile Ser Leu Asn | Ile Pro Ala Pro Gln | Pro Val Cys |
| 1550 | 1555 | 1560 | |
| Ile Ser | Glu Lys Gln Glu Asn | Asp Val Ile Asn Ala | Ile Leu Lys |
| 1565 | 1570 | 1575 | |
| Gln His | Thr Glu Glu Lys Glu | Phe Val Glu Lys His | Phe Asn Asp |
| 1580 | 1585 | 1590 | |
| Leu Asn | Met Lys Ala Val Glu | Cln Asp Glu Pro Ile | Pro Gln Lys |
| 1595 | 1600 | 1605 | |
| Pro Gln | Ser Ala Phe Tyr Tyr | Cys Arg Leu Leu Leu | Ser Ile Leu |
| 1610 | 1615 | 1620 | |
| Gly Met | Asn Ser Trp Asp Lys | Arg Arg Ser Phe His | Leu Leu Lys |
| 1625 | 1630 | 1635 | |
| Lys Asn | Glu Lys Leu Leu Arg | Glu Leu Arg Asn Leu | Asp Ser Arg |
| 1640 | 1645 | 1650 | |
| Gln Cys | Arg Glu Thr His Lys | Ile Ala Val Phe Tyr | Val Ala Glu |
| 1655 | 1660 | 1665 | |
| Gly Gln | Glu Asp Lys His Ser | Ile Leu Thr Asn Thr | Gly Gly Ser |
| 1670 | 1675 | 1680 | |
| Gln Ala | Tyr Glu Asp Phe Val | Ala Gly Leu Gly Trp | Glu Val Asn |
| 1685 | 1690 | 1695 | |
| Leu Thr | Asn His Cys Gly Phe | Met Gly Gly Leu Gln | Lys Asn Lys |
| 1700 | 1705 | 1710 | |
| Ser Thr | Gly Leu Thr Thr Pro | Tyr Phe Ala Thr Ser | Thr Val Glu |
| 1715 | 1720 | 1725 | |
| Leu Arg | His Leu Gly Asn Asp | Glu Val His Ile Val | Trp Ser Glu |
| 1730 | 1735 | 1740 | |
| His Thr | Arg Asp Tyr Arg Arg | Gly Ile Ile Pro Thr | Glu Phe Gly |
| 1745 | 1750 | 1755 | |
| Asp Val | Leu Ile Val Ile Tyr | Pro Met Lys Asn His | Met Phe Ser |

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| 1760 | 1765 | 1770 |
|--|------|------|
| Ile Gln Ile Met Lys Lys Pro Glu Val Pro Phe Phe Gly Pro Leu 1775 1780 1785 | | |
| Phe Asp Gly Ala Ile Val Asn Gly Lys Val Leu Pro Ile Met Val 1790 1795 1800 | | |
| Arg Ala Thr Ala Ile Asn Ala Ser Arg Ala Leu Lys Ser Leu Ile 1805 1810 1815 | | |
| Pro Leu Tyr Gln Asn Phe Tyr Glu Glu Arg Ala Arg Tyr Leu Gln 1820 1825 1830 | | |
| Thr Ile Val Gln His His Leu Glu Pro Thr Thr Phe Glu Asp Phe 1835 1840 1845 | | |
| Ala Ala Gln Val Phe Ser Pro Ala Pro Tyr His His Leu Pro Ser 1850 1855 1860 | | |
| Asp Ala Asp His 1865 | | |
| <210> 461 | | |
| <211> 1906 | | |
| <212> PRT | | |
| <213> Homo sapien | | |
| <400> 461 | | |
| Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His 1 5 10 15 | | |
| Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln 20 25 30 | | |
| Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln 35 40 45 | | |
| Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala 50 55 60 | | |
| Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn 65 70 75 80 | | |
| Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys 85 90 95 | | |

593

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

594

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
 420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
 435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
 450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
 465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
 485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
 500 505 510

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro

595

580

585

590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
 675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
 785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
 805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
 820 825 830

596

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
 835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
 850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
 865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
 885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
 900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
 915 920 925

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
 930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
 945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
 965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
 980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
 995 1000 1005

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe
 1010 1015 1020

Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile
 1025 1030 1035

Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu
 1040 1045 1050

Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala
 1055 1060 1065

597

| | | | | | | | | |
|---------|---------|---------|------|---------|---------|------|---------|-----|
| Ala Gly | Arg Val | Ala Ser | Ser | Ala Phe | Leu Asn | Ala | Pro Arg | Val |
| 1070 | | | 1075 | | | 1080 | | |
| Glu Ala | Gln Val | Leu Leu | Gly | Ser Leu | Val Cys | Phe | Pro Asn | Leu |
| 1085 | | | 1090 | | | 1095 | | |
| Tyr Cys | Glu Leu | Pro Ser | Leu | His Pro | Asn Ile | Pro | Asp Val | Ala |
| 1100 | | | 1105 | | | 1110 | | |
| Val Ser | Gln Phe | Thr Asp | Val | Lys Glu | Leu Ile | Ile | Lys Thr | Val |
| 1115 | | | 1120 | | | 1125 | | |
| Leu Ser | Ser Ala | Arg Asp | Glu | Pro Ser | Gly Pro | Ala | Arg Cys | Val |
| 1130 | | | 1135 | | | 1140 | | |
| Ala Leu | Cys Ser | Leu Gly | Ile | Trp Ile | Cys Glu | Glu | Leu Val | His |
| 1145 | | | 1150 | | | 1155 | | |
| Glu Ser | His His | Pro Gln | Ile | Lys Glu | Ala Leu | Asn | Val Ile | Cys |
| 1160 | | | 1165 | | | 1170 | | |
| Val Ser | Leu Lys | Phe Thr | Asn | Lys Thr | Val Ala | His | Val Ala | Cys |
| 1175 | | | 1180 | | | 1185 | | |
| Asn Met | Leu His | Met Leu | Val | His Tyr | Val Pro | Arg | Leu Gln | Ile |
| 1190 | | | 1195 | | | 1200 | | |
| Tyr Gln | Pro Asp | Ser Pro | Leu | Lys Ile | Ile Gln | Ile | Leu Ile | Ala |
| 1205 | | | 1210 | | | 1215 | | |
| Thr Ile | Thr His | Leu Leu | Pro | Ser Thr | Glu Ala | Ser | Ser Tyr | Glu |
| 1220 | | | 1225 | | | 1230 | | |
| Met Asp | Lys Arg | Leu Val | Val | Ser Leu | Leu Leu | Cys | Leu Leu | Asp |
| 1235 | | | 1240 | | | 1245 | | |
| Trp Ile | Met Ala | Leu Pro | Leu | Lys Thr | Leu Leu | Gln | Pro Phe | His |
| 1250 | | | 1255 | | | 1260 | | |
| Ala Thr | Gly Ala | Glu Ser | Asp | Lys Thr | Glu Lys | Ser | Val Leu | Asn |
| 1265 | | | 1270 | | | 1275 | | |
| Cys Ile | Tyr Lys | Val Leu | His | Gly Cys | Val Tyr | Gly | Ala Gln | Cys |
| 1280 | | | 1285 | | | 1290 | | |

598

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Phe | Ser | Asn | Pro | Arg | Tyr | Phe | Pro | Met | Ser | Leu | Ser | Asp | Leu | Ala |
| 1295 | | | | | | 1300 | | | | | 1305 | | | |
| Ser | Val | Asp | Tyr | Asp | Pro | Phe | Met | His | Leu | Glu | Ser | Leu | Lys | Glu |
| 1310 | | | | | | 1315 | | | | | 1320 | | | |
| Pro | Glu | Pro | Leu | His | Ser | Pro | Asp | Ser | Glu | Arg | Ser | Ser | Lys | Leu |
| 1325 | | | | | | 1330 | | | | | 1335 | | | |
| Gln | Pro | Val | Thr | Glu | Val | Lys | Thr | Gln | Met | Gln | His | Gly | Leu | Ile |
| 1340 | | | | | | 1345 | | | | | 1350 | | | |
| Ser | Ile | Ala | Ala | Arg | Thr | Val | Ile | Thr | His | Leu | Val | Asn | His | Leu |
| 1355 | | | | | | 1360 | | | | | 1365 | | | |
| Gly | His | Tyr | Pro | Met | Ser | Gly | Gly | Pro | Ala | Met | Leu | Thr | Ser | Gln |
| 1370 | | | | | | 1375 | | | | | 1380 | | | |
| Val | Cys | Glu | Asn | His | Asp | Asn | His | Tyr | Ser | Glu | Ser | Thr | Glu | Leu |
| 1385 | | | | | | 1390 | | | | | 1395 | | | |
| Ser | Pro | Glu | Leu | Phe | Glu | Ser | Pro | Asn | Ile | Gln | Phe | Phe | Val | Leu |
| 1400 | | | | | | 1405 | | | | | 1410 | | | |
| Asn | Asn | Thr | Thr | Leu | Val | Ser | Cys | Ile | Gln | Ile | Arg | Ser | Glu | Glu |
| 1415 | | | | | | 1420 | | | | | 1425 | | | |
| Asn | Met | Pro | Gly | Gly | Gly | Leu | Ser | Ala | Gly | Leu | Ala | Ser | Ala | Asn |
| 1430 | | | | | | 1435 | | | | | 1440 | | | |
| Ser | Asn | Val | Arg | Ile | Ile | Val | Arg | Asp | Leu | Ser | Gly | Lys | Tyr | Ser |
| 1445 | | | | | | 1450 | | | | | 1455 | | | |
| Trp | Asp | Ser | Ala | Ile | Leu | Tyr | Gly | Pro | Pro | Pro | Val | Ser | Gly | Leu |
| 1460 | | | | | | 1465 | | | | | 1470 | | | |
| Ser | Glu | Pro | Thr | Ser | Phe | Met | Leu | Ser | Leu | Ser | His | Gln | Glu | Lys |
| 1475 | | | | | | 1480 | | | | | 1485 | | | |
| Pro | Glu | Glu | Pro | Pro | Thr | Ser | Asn | Glu | Cys | Leu | Glu | Asp | Ile | Thr |
| 1490 | | | | | | 1495 | | | | | 1500 | | | |
| Val | Lys | Asp | Gly | Leu | Ser | Leu | Gln | Phe | Lys | Arg | Phe | Arg | Glu | Thr |
| 1505 | | | | | | 1510 | | | | | 1515 | | | |
| Val | Pro | Thr | Trp | Asp | Thr | Ile | Arg | Asp | Glu | Glu | Asp | Val | Leu | Asp |

599

| | | |
|---|------|------|
| 1520 | 1525 | 1530 |
| Glu Leu Leu Gln Tyr Leu Gly Val Thr Ser Pro Glu Cys Leu Gln | | |
| 1535 | 1540 | 1545 |
| Arg Thr Gly Ile Ser Leu Asn Ile Pro Ala Pro Gln Pro Val Cys | | |
| 1550 | 1555 | 1560 |
| Ile Ser Glu Lys Gln Glu Asn Asp Val Ile Asn Ala Ile Leu Lys | | |
| 1565 | 1570 | 1575 |
| Gln His Thr Glu Glu Lys Glu Phe Val Glu Lys His Phe Asn Asp | | |
| 1580 | 1585 | 1590 |
| Leu Asn Met Lys Ala Val Glu Gln Asp Glu Pro Ile Pro Gln Lys | | |
| 1595 | 1600 | 1605 |
| Pro Gln Ser Ala Phe Tyr Tyr Cys Arg Leu Leu Leu Ser Ile Leu | | |
| 1610 | 1615 | 1620 |
| Gly Met Asn Ser Trp Asp Lys Arg Arg Ser Phe His Leu Leu Lys | | |
| 1625 | 1630 | 1635 |
| Lys Asn Glu Lys Leu Leu Arg Glu Leu Arg Asn Leu Asp Ser Arg | | |
| 1640 | 1645 | 1650 |
| Gln Cys Arg Glu Thr His Lys Ile Ala Val Phe Tyr Val Ala Glu | | |
| 1655 | 1660 | 1665 |
| Gly Gln Glu Asp Lys His Ser Ile Leu Thr Asn Thr Gly Gly Ser | | |
| 1670 | 1675 | 1680 |
| Gln Ala Tyr Glu Asp Phe Val Ala Gly Leu Gly Trp Glu Val Asn | | |
| 1685 | 1690 | 1695 |
| Leu Thr Asn His Cys Gly Phe Met Gly Gly Leu Gln Lys Asn Lys | | |
| 1700 | 1705 | 1710 |
| Ser Thr Gly Leu Thr Thr Pro Tyr Phe Ala Thr Ser Thr Val Glu | | |
| 1715 | 1720 | 1725 |
| Val Ile Phe His Val Ser Thr Arg Met Pro Ser Asp Ser Asp Asp | | |
| 1730 | 1735 | 1740 |
| Ser Leu Thr Lys Lys Leu Arg His Leu Gly Asn Asp Glu Val His | | |
| 1745 | 1750 | 1755 |

600

Ile Val Trp Ser Glu His Thr Arg Asp Tyr Arg Arg Gly Ile Ile
 1760 1765 1770

Pro Thr Glu Phe Gly Asp Val Leu Ile Val Ile Tyr Pro Met Lys
 1775 1780 1785

Asn His Met Phe Ser Ile Gln Ile Met Lys Lys Pro Glu Val Pro
 1790 1795 1800

Phe Phe Gly Pro Leu Phe Asp Gly Ala Ile Val Asn Gly Lys Val
 1805 1810 1815

Leu Pro Ile Met Val Arg Ala Thr Ala Ile Asn Ala Ser Arg Ala
 1820 1825 1830

Leu Lys Ser Leu Ile Pro Leu Tyr Gln Asn Leu Arg Arg Glu His
 1835 1840 1845

Asp Ile Phe Lys Cys Cys Trp Phe Tyr Val Val Leu Asp Asn Cys
 1850 1855 1860

Leu Gln Val Ser Cys Ser His His Leu Glu Pro Thr Thr Phe Glu
 1865 1870 1875

Asp Phe Ala Ala Gln Val Phe Ser Pro Ala Pro Tyr His His Leu
 1880 1885 1890

Pro Ser Asp Ala Gly Leu Leu Pro Arg Asp Ser Thr Gln
 1895 1900 1905

<210> 462

<211> 1889

<212> PRT

<213> Homo sapien

<400> 462

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

601

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu

602

| | | |
|---|-----|-------------|
| 290 | 295 | 300 |
| Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr | | |
| 305 | 310 | 315 320 |
| Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn | | |
| | 325 | 330 335 |
| Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn | | |
| | 340 | 345 350 |
| Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu | | |
| | 355 | 360 365 |
| Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile | | |
| | 370 | 375 380 |
| Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn | | |
| | 385 | 390 395 400 |
| Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr | | |
| | 405 | 410 415 |
| Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln | | |
| | 420 | 425 430 |
| Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro | | |
| | 435 | 440 445 |
| Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala | | |
| | 450 | 455 460 |
| Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile | | |
| | 465 | 470 475 480 |
| Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu | | |
| | 485 | 490 495 |
| Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu | | |
| | 500 | 505 510 |
| Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu | | |
| | 515 | 520 525 |
| Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln | | |
| | 530 | 535 540 |

603

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Val Asn Lys Glu Asp Met Ser Gln Lys Leu
 660 665 670

Pro Pro Leu Asn Ser Asp Ile Gly Gly Ser Ser Ala Asn Val Pro Asp
 675 680 685

Leu Met Asp Glu Phe Ile Ala Glu Arg Leu Arg Ser Gly Asn Ala Ser
 690 695 700

Thr Met Thr Arg Arg Gly Ser Ser Pro Gly Ser Leu Glu Ile Pro Lys
 705 710 715 720

Asp Leu Pro Asp Ile Leu Asn Lys Gln Asn Gln Met Arg Pro Ile Asp
 725 730 735

Asp Pro Gly Val Pro Ser Glu Trp Thr Ser Pro Ala Ser Ala Gly Ser
 740 745 750

Ser Asp Leu Ile Ser Ser Asp Ser His Ser Asp Ser Phe Ser Ala Phe
 755 760 765

Gln Tyr Asp Gly Arg Lys Phe Asp Asn Phe Gly Phe Gly Thr Asp Thr
 770 775 780

604

Gly Val Thr Ser Ser Ala Asp Val Asp Ser Gly Ser Gly His His Gln
785 790 795 800

Ser Ala Glu Glu Gln Glu Val Ala Ser Leu Thr Thr Leu His Ile Asp
805 810 815

Ser Glu Thr Ser Ser Leu Asn Gln Gln Ala Phe Ser Ala Glu Val Ala
820 825 830

Thr Ile Thr Gly Ser Glu Ser Ala Ser Pro Val His Ser Pro Leu Gly
835 840 845

Ser Arg Ser Gln Thr Pro Ser Pro Ser Thr Leu Asn Ile Asp His Met
850 855 860

Glu Gln Lys Asp Leu Gln Leu Asp Glu Lys Leu His His Ser Val Leu
865 870 875 880

Gln Thr Pro Asp Asp Leu Glu Ile Ser Glu Phe Pro Ser Glu Cys Cys
885 890 895

Ser Val Met Ala Gly Gly Thr Leu Thr Gly Trp His Ala Asp Val Ala
900 905 910

Thr Val Met Trp Arg Arg Met Leu Gly Ile Leu Gly Asp Val Asn Ser
915 920 925

Ile Met Asp Pro Glu Ile His Ala Gln Val Phe Asp Tyr Leu Cys Glu
930 935 940

Leu Trp Gln Asn Leu Ala Lys Ile Arg Asp Asn Leu Gly Ile Ser Thr
945 950 955 960

Asp Asn Leu Thr Ser Pro Ser Pro Pro Val Leu Ile Pro Pro Leu Arg
965 970 975

Ile Leu Thr Pro Trp Leu Phe Lys Ala Thr Met Leu Thr Asp Lys Tyr
980 985 990

Lys Gln Gly Lys Leu His Ala Tyr Lys Leu Ile Cys Asn Thr Met Lys
995 1000 1005

Arg Arg Gln Asp Val Ser Pro Asn Arg Asp Phe Leu Thr His Phe
1010 1015 1020

605

Tyr Asn Ile Met His Cys Gly Leu Leu His Ile Asp Gln Asp Ile
 1025 1030 1035

Val Asn Thr Ile Ile Lys His Cys Ser Pro Gln Phe Phe Ser Leu
 1040 1045 1050

Gly Leu Pro Gly Ala Thr Met Leu Ile Met Asp Phe Ile Val Ala
 1055 1060 1065

Ala Gly Arg Val Ala Ser Ser Ala Phe Leu Asn Ala Pro Arg Val
 1070 1075 1080

Glu Ala Gln Val Leu Leu Gly Ser Leu Val Cys Phe Pro Asn Leu
 1085 1090 1095

Tyr Cys Glu Leu Pro Ser Leu His Pro Asn Ile Pro Asp Val Ala
 1100 1105 1110

Val Ser Gln Phe Thr Asp Val Lys Glu Leu Ile Ile Lys Thr Val
 1115 1120 1125

Leu Ser Ser Ala Arg Asp Glu Pro Ser Gly Pro Ala Arg Cys Val
 1130 1135 1140

Ala Leu Cys Ser Leu Gly Ile Trp Ile Cys Glu Glu Leu Val His
 1145 1150 1155

Glu Ser His His Pro Gln Ile Lys Glu Ala Leu Asn Val Ile Cys
 1160 1165 1170

Val Ser Leu Lys Phe Thr Asn Lys Thr Val Ala His Val Ala Cys
 1175 1180 1185

Asn Met Leu His Met Leu Val His Tyr Val Pro Arg Leu Gln Ile
 1190 1195 1200

Tyr Gln Pro Asp Ser Pro Leu Lys Ile Ile Gln Ile Leu Ile Ala
 1205 1210 1215

Thr Ile Thr His Leu Leu Pro Ser Thr Glu Ala Ser Ser Tyr Glu
 1220 1225 1230

Met Asp Lys Arg Leu Val Val Ser Leu Leu Leu Cys Leu Leu Asp
 1235 1240 1245

Trp Ile Met Ala Leu Pro Leu Lys Thr Leu Leu Gln Pro Phe His

606

| | | |
|---|------|------|
| 1250 | 1255 | 1260 |
| Ala Thr Gly Ala Glu Ser Asp Lys Thr Glu Lys Ser Val Leu Asn | | |
| 1265 | 1270 | 1275 |
| Cys Ile Tyr Lys Val Leu His Gly Cys Val Tyr Gly Ala Gln Cys | | |
| 1280 | 1285 | 1290 |
| Phe Ser Asn Pro Arg Tyr Phe Pro Met Ser Leu Ser Asp Leu Ala | | |
| 1295 | 1300 | 1305 |
| Ser Val Asp Tyr Asp Pro Phe Met His Leu Glu Ser Leu Lys Glu | | |
| 1310 | 1315 | 1320 |
| Pro Glu Pro Leu His Ser Pro Asp Ser Glu Arg Ser Ser Lys Leu | | |
| 1325 | 1330 | 1335 |
| Gln Pro Val Thr Glu Val Lys Thr Gln Met Gln His Gly Leu Ile | | |
| 1340 | 1345 | 1350 |
| Ser Ile Ala Ala Arg Thr Val Ile Thr His Leu Val Asn His Leu | | |
| 1355 | 1360 | 1365 |
| Gly His Tyr Pro Met Ser Gly Gly Pro Ala Met Leu Thr Ser Gln | | |
| 1370 | 1375 | 1380 |
| Val Cys Glu Asn His Asp Asn His Tyr Ser Glu Ser Thr Glu Leu | | |
| 1385 | 1390 | 1395 |
| Ser Pro Glu Leu Phe Glu Ser Pro Asn Ile Gln Phe Phe Val Leu | | |
| 1400 | 1405 | 1410 |
| Asn Asn Thr Thr Leu Val Ser Cys Ile Gln Ile Arg Ser Glu Glu | | |
| 1415 | 1420 | 1425 |
| Asn Met Pro Gly Gly Gly Leu Ser Ala Gly Leu Ala Ser Ala Asn | | |
| 1430 | 1435 | 1440 |
| Ser Asn Val Arg Ile Ile Val Arg Asp Leu Ser Gly Lys Tyr Ser | | |
| 1445 | 1450 | 1455 |
| Trp Asp Ser Ala Ile Leu Tyr Gly Pro Pro Pro Val Ser Gly Leu | | |
| 1460 | 1465 | 1470 |
| Ser Glu Pro Thr Ser Phe Met Leu Ser Leu Ser His Gln Glu Lys | | |
| 1475 | 1480 | 1485 |

607

| | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|
| Pro | Glu | Glu | Pro | Pro | Thr | Ser | Asn | Glu | Cys | Leu | Glu | Asp | Ile | Thr |
| 1490 | | | | | | 1495 | | | | | 1500 | | | |
| Val | Lys | Asp | Gly | Leu | Ser | Leu | Gln | Phe | Lys | Arg | Phe | Arg | Glu | Thr |
| 1505 | | | | | | 1510 | | | | | 1515 | | | |
| Val | Pro | Thr | Trp | Asp | Thr | Ile | Arg | Asp | Glu | Glu | Asp | Val | Leu | Asp |
| 1520 | | | | | | 1525 | | | | | 1530 | | | |
| Glu | Leu | Leu | Gln | Tyr | Leu | Gly | Val | Thr | Ser | Pro | Glu | Cys | Leu | Gln |
| 1535 | | | | | | 1540 | | | | | 1545 | | | |
| Arg | Thr | Gly | Ile | Ser | Leu | Asn | Ile | Pro | Ala | Pro | Gln | Pro | Val | Cys |
| 1550 | | | | | | 1555 | | | | | 1560 | | | |
| Ile | Ser | Glu | Lys | Gln | Glu | Asn | Asp | Val | Ile | Asn | Ala | Ile | Leu | Lys |
| 1565 | | | | | | 1570 | | | | | 1575 | | | |
| Gln | His | Thr | Glu | Glu | Lys | Glu | Phe | Val | Glu | Lys | His | Phe | Asn | Asp |
| 1580 | | | | | | 1585 | | | | | 1590 | | | |
| Leu | Asn | Met | Lys | Ala | Val | Glu | Gln | Asp | Glu | Pro | Ile | Pro | Gln | Lys |
| 1595 | | | | | | 1600 | | | | | 1605 | | | |
| Pro | Gln | Ser | Ala | Phe | Tyr | Tyr | Cys | Arg | Leu | Leu | Leu | Ser | Ile | Leu |
| 1610 | | | | | | 1615 | | | | | 1620 | | | |
| Gly | Met | Asn | Ser | Trp | Asp | Lys | Arg | Arg | Ser | Phe | His | Leu | Leu | Lys |
| 1625 | | | | | | 1630 | | | | | 1635 | | | |
| Lys | Asn | Glu | Lys | Leu | Leu | Arg | Glu | Leu | Arg | Asn | Leu | Asp | Ser | Arg |
| 1640 | | | | | | 1645 | | | | | 1650 | | | |
| Gln | Cys | Arg | Glu | Thr | His | Lys | Ile | Ala | Val | Phe | Tyr | Val | Ala | Glu |
| 1655 | | | | | | 1660 | | | | | 1665 | | | |
| Gly | Gln | Glu | Asp | Lys | His | Ser | Ile | Leu | Thr | Asn | Thr | Gly | Gly | Ser |
| 1670 | | | | | | 1675 | | | | | 1680 | | | |
| Gln | Ala | Tyr | Glu | Asp | Phe | Val | Ala | Gly | Leu | Gly | Trp | Glu | Val | Asn |
| 1685 | | | | | | 1690 | | | | | 1695 | | | |
| Leu | Thr | Asn | His | Cys | Gly | Phe | Met | Gly | Gly | Leu | Gln | Lys | Asn | Lys |
| 1700 | | | | | | 1705 | | | | | 1710 | | | |

608

Ser Thr Gly Leu Thr Thr Pro Tyr Phe Ala Thr Ser Thr Val Glu
1715 1720 1725

Val Ile Phe His Val Ser Thr Arg Met Pro Ser Asp Ser Asp Asp
1730 1735 1740

Ser Leu Thr Lys Lys Leu Arg His Leu Gly Asn Asp Glu Val His
1745 1750 1755

Ile Val Trp Ser Glu His Thr Arg Asp Tyr Arg Arg Gly Ile Ile
1760 1765 1770

Pro Thr Glu Phe Gly Asp Val Leu Ile Val Ile Tyr Pro Met Lys
1775 1780 1785

Asn His Met Phe Ser Ile Gln Ile Met Lys Lys Pro Glu Val Pro
1790 1795 1800

Phe Phe Gly Pro Leu Phe Asp Gly Ala Ile Val Asn Gly Lys Val
1805 1810 1815

Leu Pro Ile Met Val Arg Ala Thr Ala Ile Asn Ala Ser Arg Ala
1820 1825 1830

Leu Lys Ser Leu Ile Pro Leu Tyr Gln Asn Phe Leu Phe Ser Leu
1835 1840 1845

Lys Leu Cys Tyr Ser Asn Val Gln Tyr Leu Leu Gln Ser Arg Lys
1850 1855 1860

Ala Lys Thr Lys Trp Asn Gly Ile Asp Glu Leu Ile Gly Ser Ala
1865 1870 1875

Asn Ala Val Ala Phe Arg Tyr Asn Lys Thr Leu
1880 1885

<210> 463

<211> 861

<212> PRT

<213> Homo sapien

<400> 463

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln

609

20

25

30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

610

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr
305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
340 345 350

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp Glu Gln
420 425 430

Met Leu Leu Val Leu Leu Arg Val Thr Glu Ser Val Leu Lys Met Pro
435 440 445

Ser Gln Ala Phe Leu Gln Phe Gln Gly Lys Lys Asn Met Thr Leu Ala
450 455 460

Gly Arg Leu Ala Gly Pro Leu Phe Gln Thr Leu Ile Val Ala Trp Ile
465 470 475 480

Lys Ala Asn Leu Asn Val Tyr Ile Ser Arg Glu Leu Trp Asp Asp Leu
485 490 495

Leu Ser Val Leu Ser Ser Leu Thr Tyr Trp Glu Glu Leu Ala Thr Glu
500 505 510

611

Trp Ser Leu Thr Met Glu Thr Leu Thr Lys Val Leu Ala Arg Asn Leu
 515 520 525

Tyr Ser Leu Asp Leu Ser Asp Leu Pro Leu Asp Lys Leu Ser Glu Gln
 530 535 540

Lys Gln Lys Lys His Lys Gly Lys Gly Val Gly His Glu Phe Gln Lys
 545 550 555 560

Val Ser Val Asp Lys Ser Phe Ser Arg Gly Trp Ser Arg Asp Gln Pro
 565 570 575

Gly Gln Ala Pro Met Arg Gln Arg Ser Ala Thr Thr Thr Gly Ser Pro
 580 585 590

Gly Thr Glu Lys Ala Arg Ser Ile Val Arg Gln Lys Thr Val Asp Ile
 595 600 605

Asp Asp Ala Gln Ile Leu Pro Arg Ser Thr Arg Val Arg His Phe Ser
 610 615 620

Gln Ser Glu Glu Thr Gly Asn Glu Val Phe Gly Ala Leu Asn Glu Glu
 625 630 635 640

Gln Pro Leu Pro Arg Ser Ser Ser Thr Ser Asp Ile Leu Glu Pro Phe
 645 650 655

Thr Val Glu Arg Ala Lys Gly Ala Val Pro Val Ile Asp Ser Ser Ser
 660 665 670

Arg His Ala Pro Ser Leu Gln Ser Ser Thr Glu Ala Ser Ser Ile Thr
 675 680 685

Arg Ser Thr Glu Ser His Ile Thr Asp Thr His Ser Arg Glu Ser Ser
 690 695 700

Leu Glu Val Gly Asp Ser Ile Tyr Asp His Leu Cys His Leu Ile Gly
 705 710 715 720

Pro Val Glu Leu Ala Asp Ser Ala Phe Glu Gln Ile Gln Tyr Ile Asp
 725 730 735

Leu Glu Gly Asp Asp Asp Leu Leu Ser Thr Leu Lys Glu Tyr Phe Lys
 740 745 750

612

Glu Asn Gln Glu Asn His Ser Lys Asn Glu Thr Gly Lys Asp Pro Ala
 755 760 765

Ser Gln Glu Val Thr Ile Ala Val Asn Arg Gly Glu Arg Leu Ser Leu
 770 775 780

Asp Lys Leu Glu Cys Thr Asp Gln Glu Thr Glu Ser Glu Asn Ile Thr
 785 790 795 800

Ser Phe Val Gly Thr Pro Glu Asn Leu Gln Phe Gln Lys Glu Pro Asn
 805 810 815

Ser Ala Val Phe Met Ser Asn Ile Ala Pro Asn Gln Ser Asp Ser Phe
 820 825 830

Phe Arg Thr Gln Thr Ser Glu Lys Ser Lys Gln Leu Asn Thr Asp Lys
 835 840 845

Gln Pro Ser Glu Pro Ser Leu Asp Ser Pro Cys Asp Lys
 850 855 860

<210> 464
 <211> 430
 <212> PRT
 <213> Homo sapien

<400> 464

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

613

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys
 130 135 140

Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu
 145 150 155 160

Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro
 165 170 175

Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala
 180 185 190

Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr
 195 200 205

Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu
 210 215 220

Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu
 225 230 235 240

His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg
 245 250 255

Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu
 260 265 270

Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln
 275 280 285

Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu
 290 295 300

Glu Ile Val Ile Thr Ser Ser Asp Ile Pro Cys Ile Glu Asn Val Thr
 305 310 315 320

Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn
 325 330 335

Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn
 340 345 350

614

Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu
 355 360 365

Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Phe Ile Ile
 370 375 380

Asn Ser Ser Asn Ile Phe Leu Leu Glu Pro Ala Asn Glu Ile Lys Asn
 385 390 395 400

Leu Leu Asp Glu His Thr Asp Met Cys Lys Arg Ile Leu Asn Ile Tyr
 405 410 415

Arg Tyr Met Val Val Gln Val Ser Met Asp Lys Lys Thr Trp
 420 425 430

<210> 465
 <211> 417
 <212> PRT
 <213> Homo sapien

<400> 465

Met Phe Ser Cys Leu Ile Pro Gly Phe Ser Ala Pro Gln Ser Glu His
 1 5 10 15

Gly Pro Arg Thr Leu Asp Asn Leu Ile Asn Pro Pro Leu Asn Leu Gln
 20 25 30

Glu Thr Gln Val Thr Ile Glu Glu Ile Thr Pro Leu Val Pro Pro Gln
 35 40 45

Ser Gly Asp Lys Gly Gln Glu Asp Leu Thr Ser Tyr Phe Leu Glu Ala
 50 55 60

Leu Leu Lys Tyr Ile Val Ile Gln Val Lys Ser Leu Glu Trp Lys Asn
 65 70 75 80

Lys Glu Asn Gln Glu Arg Gly Phe Ser Phe Leu Phe Ser His Phe Lys
 85 90 95

Lys Tyr Tyr Leu Pro Tyr Ile Phe Pro Asn Ile Cys Lys Glu Asn Ser
 100 105 110

Leu Tyr His Pro Ile Leu Asp Ile Pro Gln Met Arg Pro Lys Pro His
 115 120 125

Tyr Val Val Ile Lys Lys Asp Ala Glu Thr Asn Glu Ala Ile Tyr Cys

615

| | | |
|--|-----|-----|
| 130 | 135 | 140 |
| Thr Lys Glu Pro Phe Ile Lys Ala Arg Val Ile Val Ile Arg Trp Leu 145 150 155 160 | | |
| Val Ser Phe Trp Leu Glu Pro Lys Pro His Thr Gly Pro His Ile Pro 165 170 175 | | |
| Gly Met Glu Gly Glu Val Leu Pro Lys Asn Ile Gln Arg Ala Ala Ala 180 185 190 | | |
| Ser Leu Val Ser Arg Glu Glu Ser Lys Asn Asp Asn Ala Asp Lys Thr 195 200 205 | | |
| Asp Arg Thr Thr Glu Pro Glu Gln Ser His Ser Asn Thr Ser Thr Leu 210 215 220 | | |
| Thr Glu Arg Glu Pro Ser Ser Ser Ser Leu Cys Ser Ile Asp Glu Glu 225 230 235 240 | | |
| His Leu Thr Asp Ile Glu Ile Val Arg Arg Val Phe Ser Ser Lys Arg 245 250 255 | | |
| Ser Asn Val Asn Phe Val Thr Glu Ile Phe Arg Gln Ala Phe Leu Leu 260 265 270 | | |
| Pro Ile Cys Glu Ala Ala Ala Met Arg Lys Val Val Lys Val Tyr Gln 275 280 285 | | |
| Glu Trp Ile Gln Gln Glu Glu Lys Pro Leu Phe Met Gln Glu Pro Glu 290 295 300 | | |
| Glu Ile Val Ile Thr Ser Ser Asp Leu Pro Cys Ile Glu Asn Val Thr 305 310 315 320 | | |
| Asp His Asp Ile Ser Met Glu Glu Gly Glu Lys Arg Glu Glu Glu Asn 325 330 335 | | |
| Gly Thr Asn Thr Ala Asp His Val Arg Asn Ser Ser Trp Ala Lys Asn 340 345 350 | | |
| Gly Ser Tyr Gln Gly Ala Leu His Asn Ala Ser Glu Glu Ala Thr Glu 355 360 365 | | |
| Gln Asn Ile Arg Ala Gly Thr Gln Ala Val Leu Gln Val Asp His Phe 370 375 380 | | |

616

Met Ala Ile Phe Lys Asn Lys Ile Ile Ile Lys Tyr Phe Cys Ser Val
 385 390 395 400

Phe Gln Tyr Thr Val Tyr Phe Ser Gln Tyr Asn Lys Phe Thr Thr Tyr
 405 410 415

Ile

<210> 466
 <211> 76
 <212> PRT
 <213> Homo sapien

<400> 466

Met Asn Arg Phe Lys Glu Gly Phe Lys Asn Ser Trp Ile Thr His Pro
 1 5 10 15

Pro Trp Thr Ile Ile Gly Ser Gln Arg Ser Gly Ala Tyr His Lys Ala
 20 25 30

His Arg Ala Ala Ser Met Lys Asn Ala Ser Thr Asn Gly Cys Pro Leu
 35 40 45

Ser Glu Thr Glu Tyr Trp Ala Arg Arg Asp Pro Ile Pro Ala Asn Gly
 50 55 60

Ala Phe Leu Arg Leu Ser Arg His Lys Thr Ser His
 65 70 75

<210> 467
 <211> 198
 <212> PRT
 <213> Homo sapien

<400> 467

Met Phe Lys Asn Thr Phe Gln Ser Gly Phe Leu Ser Ile Leu Tyr Ser
 1 5 10 15

Ile Gly Ser Lys Pro Leu Gln Ile Trp Asp Lys Lys Val Arg Asn Gly
 20 25 30

His Ile Lys Arg Ile Thr Asp Asn Asp Ile Gln Ser Leu Val Leu Glu
 35 40 45

Ile Glu Gly Thr Asn Val Ser Thr Thr Tyr Ile Thr Cys Pro Ala Asp

617

50

55

60

Pro Lys Lys Thr Leu Gly Ile Lys Leu Pro Phe Leu Val Met Ile Ile
 65 70 75 80

Lys Asn Leu Lys Lys Tyr Phe Thr Phe Glu Val Gln Val Leu Asp Asp
 85 90 95

Lys Asn Val Arg Arg Arg Phe Arg Ala Ser Asn Tyr Gln Ser Thr Thr
 100 105 110

Arg Val Lys Pro Phe Ile Cys Thr Met Pro Met Arg Leu Asp Asp Gly
 115 120 125

Trp Asn Gln Ile Gln Phe Asn Leu Leu Asp Phe Thr Arg Arg Ala Tyr
 130 135 140

Gly Thr Asn Tyr Ile Glu Thr Leu Arg Val Gln Asn Pro Ser Leu Arg
 145 150 155 160

Gln Ala Lys Glu Met Pro Glu Met Thr Arg Phe Gln Ser Trp Lys Arg
 165 170 175

Ala Ser Arg Arg Phe Arg Lys Arg Gly Arg Thr Val Thr Phe Arg Leu
 180 185 190

Ser Lys Glu Ala Leu Pro
 195

<210> 468
 <211> 266
 <212> PRT
 <213> Homo sapien

<220>
 <221> MISC_FEATURE
 <222> (18)..(18)
 <223> x= any amino acid

<400> 468

Met Ile Gln Val Gly Cys Arg Leu Thr Glu Asp Pro Trp Asp Leu Leu
 1 5 10 15

Thr Xaa Ala Arg Phe Cys Gln Cys Ile Pro Ala Glu Leu Arg Gln Asp
 20 25 30

Ala Leu Cys Ala Leu Ser Arg Thr Ser Val Leu Arg Ile Gly Asn Leu

618

35

40

45

His Ile Thr Gly Val Leu Arg Ser Ser Ile Gln Trp Gly Ile Val Ser
 50 55 60

Asn Glu Glu Gly Arg Pro Glu His His Val Leu Lys Leu Arg Ser Gln
 65 70 75 80

His Gly Phe Leu Ser Ile Leu Tyr Ser Ile Gly Ser Lys Pro Leu Gln
 85 90 95

Ile Trp Asp Lys Lys Val Arg Asn Gly His Ile Lys Arg Ile Thr Asp
 100 105 110

Asn Asp Ile Gln Ser Leu Val Leu Glu Ile Glu Gly Thr Asn Val Ser
 115 120 125

Thr Thr Tyr Ile Thr Cys Pro Ala Asp Pro Lys Lys Thr Leu Gly Ile
 130 135 140

Lys Leu Pro Phe Leu Val Met Ile Ile Lys Asn Leu Lys Lys Tyr Phe
 145 150 155 160

Thr Phe Glu Val Gln Val Leu Asp Asp Lys Asn Val Arg Arg Arg Phe
 165 170 175

Arg Ala Ser Asn Tyr Gln Ser Thr Thr Arg Val Lys Pro Phe Ile Cys
 180 185 190

Thr Met Pro Met Arg Leu Asp Asp Gly Trp Asn Gln Ile Gln Phe Asn
 195 200 205

Leu Leu Asp Phe Thr Arg Arg Ala Tyr Gly Thr Asn Tyr Ile Glu Thr
 210 215 220

Leu Arg Val Gln Ile His Ala Asn Cys Arg Ile Arg Arg Val Tyr Phe
 225 230 235 240

Ser Asp Arg Leu Tyr Ser Glu Asp Glu Leu Pro Ala Glu Phe Lys Leu
 245 250 255

Tyr Leu Pro Val Gln Asn Lys Ala Lys Gln
 260 265

<210> 469

<211> 250

619

<212> PRT

<213> Homo sapien

<400> 469

Met Phe Lys Asn Thr Phe Gln Ser Gly Phe Leu Ser Ile Leu Tyr Ser
 1 5 10 15

Ile Gly Ser Lys Pro Leu Gln Ile Trp Asp Lys Lys Val Arg Asn Gly
 20 25 30

His Ile Lys Arg Ile Thr Asp Asn Asp Ile Gln Ser Leu Val Leu Glu
 35 40 45

Ile Glu Gly Thr Asn Val Ser Thr Thr Tyr Ile Thr Cys Pro Ala Asp
 50 55 60

Pro Lys Lys Thr Leu Gly Ile Lys Leu Pro Phe Leu Val Met Ile Ile
 65 70 75 80

Lys Asn Leu Lys Lys Tyr Phe Thr Phe Glu Val Gln Val Leu Asp Asp
 85 90 95

Lys Asn Val Arg Arg Arg Phe Arg Ala Ser Asn Tyr Gln Ser Thr Thr
 100 105 110

Arg Val Lys Pro Phe Ile Cys Thr Met Pro Met Arg Leu Asp Asp Gly
 115 120 125

Trp Asn Gln Ile Gln Phe Asn Leu Leu Asp Phe Thr Arg Arg Ala Tyr
 130 135 140

Gly Thr Asn Tyr Ile Glu Thr Leu Arg Val Gln Ile His Ala Asn Cys
 145 150 155 160

Arg Ile Arg Arg Val Tyr Phe Ser Asp Arg Leu Tyr Ser Glu Asp Glu
 165 170 175

Leu Pro Ala Glu Phe Lys Leu Tyr Leu Pro Val Gln Asn Lys Ala Lys
 180 185 190

Val Ser Gln Ser Ser Pro Glu Glu Gly Pro Pro Val Ser Gly Gly Ser
 195 200 205

Cys Val Pro Gly Arg Cys Ser Gly Leu Arg Ile Gln Leu Gln Ser Leu
 210 215 220

620

Ser Val Leu Thr Leu Trp Gly Ala Phe Ile Ser Gln Asp Leu Arg Ser
 225 230 235 240

Pro Ser Ser Thr Glu Ser Gly Met Leu Leu
 245 250

<210> 470
 <211> 88
 <212> PRT
 <213> Homo sapien

<400> 470

Met Gln Ile Val Ala Ser Asp Gly Phe Thr Ser Gln Thr Asp Ser Thr
 1 5 10 15

Gln Lys Met Ser Cys Arg Gln Ser Ser Asn Cys Ile Ser Gln Phe Arg
 20 25 30

Thr Arg Gln Ser Asn Asn Trp Asn Cys Asp Ser Arg Asp Arg Pro Leu
 35 40 45

Asp Val Thr Leu Leu Phe Lys Arg Lys Leu Cys Gly Gly Arg Cys Lys
 50 55 60

Asn Ile Phe Ile Leu Val Cys Ser Ala Val Val Leu Leu Phe Ile Leu
 65 70 75 80

Gly Val Ala Cys His Gly His Arg
 85

<210> 471
 <211> 173
 <212> PRT
 <213> Homo sapien

<400> 471

Met Phe Lys Asn Thr Phe Gln Ser Gly Phe Leu Ser Ile Leu Tyr Ser
 1 5 10 15

Ile Gly Ser Lys Pro Leu Gln Ile Trp Asp Lys Lys Val Arg Asn Gly
 20 25 30

His Ile Lys Arg Ile Thr Asp Asn Asp Ile Gln Ser Leu Val Leu Glu
 35 40 45

Ile Glu Gly Thr Asn Val Ser Thr Thr Tyr Ile Thr Cys Pro Ala Asp
 50 55 60

621

Pro Lys Lys Thr Leu Gly Ile Lys Leu Pro Phe Leu Val Met Ile Ile
65 70 75 80

Lys Asn Leu Lys Lys Tyr Phe Thr Phe Glu Val Gln Val Leu Asp Asp
85 90 95

Lys Asn Val Arg Arg Arg Phe Arg Ala Ser Asn Tyr Gln Ser Thr Thr
100 105 110

Arg Val Lys Pro Phe Ile Cys Thr Met Pro Met Arg Leu Asp Asp Gly
115 120 125

Trp Asn Gln Ile Gln Phe Asn Leu Leu Asp Phe Thr Arg Arg Ala Tyr
130 135 140

Gly Thr Asn Tyr Ile Glu Thr Leu Arg Val Gln Val Leu Leu Leu Ser
145 150 155 160

Gln Ile Glu Pro Trp Val Gly Asp Arg Ala His Cys Val
165 170

<210> 472
<211> 110
<212> PRT
<213> Homo sapien

<400> 472

Met Ala Thr Ser Lys Glu Ser Leu Ile Val Leu Asp Asp Lys Asn Val
1 5 10 15

Arg Arg Arg Phe Arg Ala Ser Asn Tyr Gln Ser Thr Thr Arg Val Lys
20 25 30

Pro Phe Ile Cys Thr Met Pro Met Arg Leu Asp Asp Gly Trp Asn Gln
35 40 45

Ile Gln Phe Asn Leu Leu Asp Phe Thr Arg Arg Ala Tyr Gly Thr Asn
50 55 60

Tyr Ile Glu Thr Leu Arg Val Gln Ile His Ala Asn Cys Arg Ile Arg
65 70 75 80

Arg Val Tyr Phe Ser Asp Arg Leu Tyr Ser Glu Asp Glu Leu Pro Ala
85 90 95

Glu Phe Lys Leu Tyr Leu Pro Val Gln Asn Lys Ala Lys Gln

622

100

105

110

<210> 473
 <211> 25
 <212> PRT
 <213> Homo sapien

<400> 473

Met Arg Leu Asn Thr Phe Tyr Thr Thr Tyr Gln Lys Pro Gln Lys Ser
 1 5 10 15

Tyr Gly Asn Asn Gly Met Asn Thr Gln
 20 25

<210> 474
 <211> 50
 <212> PRT
 <213> Homo sapien

<400> 474

Met Cys Phe Cys Phe Pro Gln Glu Glu Asn His Val Asp Ser Gln Phe
 1 5 10 15

Thr Met Ser Gln Pro Val Cys Lys Ile Phe Tyr Ile Met Gly Lys Phe
 20 25 30

Ile Val Thr Gln Lys Phe Ser Val Phe Ser Leu Ser Tyr Gln Lys Leu
 35 40 45

Gln Met
 50

<210> 475
 <211> 90
 <212> PRT
 <213> Homo sapien

<400> 475

Met Leu Lys Tyr Phe Leu Ser Val Trp Trp Ser Leu Glu Val Asn Ser
 1 5 10 15

His Ala Arg Arg Arg His Gln Lys Ala Trp Gly Ser Ser Asp Arg Val
 20 25 30

Gly Ala Cys Trp Leu Thr Gly Gly Leu His Arg Arg Val Ile Arg Leu
 35 40 45

Glu Asn Phe Leu Arg Ile Pro Arg Thr Glu Ser Leu Thr Ser Phe Phe

623

50

55

60

Phe Ser Phe Phe Phe Val Phe Arg Ser Val Ala Gln Ala Glu Val Ser
 65 70 75 80

Leu Lys Ser Ala Phe Lys Ala Leu Leu Arg
 85 90

<210> 476

<211> 57

<212> PRT

<213> Homo sapien

<400> 476

Met Met Leu Tyr Phe Leu Leu Ile Phe Glu Tyr Leu Phe Trp Phe His
 1 5 10 15

Phe Lys Trp Leu Leu Ser Glu Ala Val Leu Gly Ile Gln Ser Asp Ser
 20 25 30

Ile Val Thr Leu Met Arg Leu Lys Phe Gln Gly His Ser Leu Ala Trp
 35 40 45

Val Leu Ser Lys Ala Leu Gly Gly Pro
 50 55

<210> 477

<211> 66

<212> PRT

<213> Homo sapien

<400> 477

Met Leu Gln Gly Gln Leu Ser Leu His Arg Asn Lys Thr Thr Ile Ala
 1 5 10 15

Phe Gln Gly His Gln Ser Phe Leu Gln Asn Glu Asn Lys Val Ser Pro
 20 25 30

Ala Tyr Leu Asn Ser Pro Asn Thr Leu Gly Asp Leu Ile Leu Ile Ser
 35 40 45

Ser Val Phe His Ser Asp Lys Ser Ile Gln Ser Leu Val Asn Phe Tyr
 50 55 60

Ser Ala
 65

624

<210> 478
 <211> 16
 <212> PRT
 <213> Homo sapien

<400> 478

Met Phe Gly Glu Val Phe Arg Val Gln Ile Ile Phe Ile Phe Glu Leu
 1 5 10 15

<210> 479
 <211> 152
 <212> PRT
 <213> Homo sapien

<400> 479

Met Trp Pro Thr Gly Pro Gly Pro Ser Val Arg Lys Glu Gln Ala Arg
 1 5 10 15

Pro Pro Ala Arg Arg Asn His Gln Val Gly His Leu Pro Tyr Arg His
 20 25 30

Pro Glu Val Pro Val Asp Ile Lys Thr Ser Ala Pro Ser Glu Ala Pro
 35 40 45

Gly Leu Arg Ser Gly Gln Arg Gly Gly Arg Gly Gln Gly Glu Gly Ala
 50 55 60

Ala Lys Glu Arg Arg Thr Ala Arg Gly Gly Gln Gly Ala Ser Leu Pro
 65 70 75 80

Arg Gln Gly Pro Pro Gln Pro Ser Arg Arg Leu Asp Arg Gly Ile Val
 85 90 95

Leu Arg Arg Arg Pro Ser Ser Gly Pro Ala Pro Ala Pro Pro Arg Ala
 100 105 110

Cys Tyr Trp Arg Lys Val Pro Gly Arg Ala Ala Thr Gly Arg His Ala
 115 120 125

Ala Gly Pro Ala Pro Phe Pro Thr Ser Ser Lys Ala Ala Pro Ala Leu
 130 135 140

Gly Leu Arg Gly Arg Arg Ser Gly
 145 150

<210> 480
 <211> 365
 <212> PRT

625

<213> Homo sapien

<400> 480

Met Trp Pro Thr Gly Pro Gly Pro Ser Val Arg Lys Glu Gln Ala Arg
 1 5 10 15

Pro Pro Ala Arg Arg Asn His Gln Val Gly His Leu Pro Tyr Arg His
 20 25 30

Pro Glu Val Pro Val Asp Ile Lys Thr Ser Ala Pro Ser Glu Ala Pro
 35 40 45

Gly Leu Arg Ser Gly Gln Arg Gly Gly Arg Gly Gln Gly Glu Gly Ala
 50 55 60

Ala Lys Glu Arg Arg Thr Ala Arg Gly Gly Gln Gly Ala Ser Leu Pro
 65 70 75 80

Arg Gln Gly Pro Pro Gln Pro Ser Arg Arg Leu Asp Arg Gly Ile Val
 85 90 95

Leu Arg Arg Arg Pro Ser Ser Gly Pro Ala Pro Ala Pro Pro Arg Ala
 100 105 110

Cys Tyr Trp Arg Lys Val Pro Gly Arg Ala Ala Thr Gly Arg His Ala
 115 120 125

Ala Gly Pro Ala Pro Phe Pro Thr Arg Ser Lys Ala Ala Pro Ala Leu
 130 135 140

Gly Leu Arg Gly Arg Arg Ser Gly Arg Gly Leu Gly Gly Phe Ala Gly
 145 150 155 160

Ala Gly Gly Gly Glu Ser Pro Asp Ser Pro Asp Ala Ala Arg Arg Ala
 165 170 175

Met Gly Phe Pro Ala Ala Ala Leu Leu Cys Ala Leu Cys Cys Gly Leu
 180 185 190

Leu Ala Pro Ala Ala Arg Ala Gly Tyr Ser Glu Glu Arg Cys Ser Trp
 195 200 205

Arg Gly Ser Gly Leu Thr Gln Glu Pro Gly Ser Val Gly Gln Leu Ala
 210 215 220

Leu Ala Cys Ala Glu Gly Ala Val Glu Trp Leu Tyr Pro Ala Gly Ala

626

| 225 | | | | | 230 | | | | | | 235 | | | | | 240 |
|---|-------------|---|-----|-----------------------------|-----|--|----|----|----|----|-----|----|----|----|--|-----|
| Leu Arg Leu Thr | 245 | Leu Gly Gly Pro Asp | 250 | Pro Arg Ala Arg Pro Gly Ile | 255 | | | | | | | | | | | |
| Ala Cys Leu Arg | 260 | Pro Val Arg Pro Phe Ala Gly Ala Gln Val Phe Ala | 265 | | 270 | | | | | | | | | | | |
| Glu Arg Ala Gly Gly Ala Leu Glu Leu Leu Leu Ala Glu Gly Pro Gly | 275 | | 280 | | | | | | | | | | | | | |
| Pro Ala Gly Gly Arg Cys Val Arg Trp Gly Pro Arg Glu Arg Arg Ala | 290 | | 295 | | | | | | | | | | | | | |
| Leu Phe Leu Gln Ala Thr Pro His Gln Asp Ile Ser Arg Arg Val Ala | 305 | | 310 | | | | | | | | | | | | | 320 |
| Ala Phe Arg Phe Glu Leu Arg Glu Asp Gly Arg Pro Glu Leu Pro Pro | | | 325 | | | | | | | | | | | | | |
| Gln Ala His Gly Leu Gly Val Asp Gly Ala Cys Arg Pro Cys Ser Asp | | | 340 | | | | | | | | | | | | | |
| Ala Glu Leu Leu Ala Ala Cys Thr Ser Asp Phe Gly | | | 355 | | | | | | | | | | | | | |
| <210> | 481 | | | | | | | | | | | | | | | |
| <211> | 332 | | | | | | | | | | | | | | | |
| <212> | PRT | | | | | | | | | | | | | | | |
| <213> | Homo sapien | | | | | | | | | | | | | | | |
| <400> | 481 | | | | | | | | | | | | | | | |
| Met Gly Phe Pro Ala Ala Ala Leu Leu Cys Ala Leu Cys Cys Gly Leu | 1 | | 5 | | | | | | 10 | | | | | | | 15 |
| Leu Ala Pro Ala Ala Arg Ala Gly Tyr Ser Glu Glu Arg Cys Ser Trp | | | 20 | | | | | 25 | | | | | | 30 | | |
| Arg Gly Ser Gly Leu Thr Gln Glu Pro Gly Ser Val Gly Gln Leu Ala | | | 35 | | | | 40 | | | | | | 45 | | | |
| Leu Ala Cys Ala Glu Gly Ala Val Glu Trp Leu Tyr Pro Ala Gly Ala | | | 50 | | | | 55 | | | | | 60 | | | | |
| Leu Arg Leu Thr Leu Gly Gly Pro Asp Pro Arg Ala Arg Pro Gly Ile | 65 | | | | 70 | | | | | 75 | | | | | | 80 |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Ala | Cys | Leu | Arg | Pro | Val | Arg | Pro | Phe | Ala | Gly | Ala | Gln | Val | Phe | Ala | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| Glu | Arg | Ala | Gly | Gly | Ala | Leu | Glu | Leu | Leu | Leu | Ala | Glu | Gly | Pro | Gly | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| Pro | Ala | Gly | Gly | Arg | Cys | Val | Arg | Trp | Gly | Pro | Arg | Glu | Arg | Arg | Ala | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| Leu | Phe | Leu | Gln | Ala | Thr | Pro | His | Gln | Asp | Ile | Ser | Arg | Arg | Val | Ala | |
| | 130 | | | | | 135 | | | | | 140 | | | | | |
| Ala | Phe | Arg | Phe | Glu | Leu | Arg | Glu | Asp | Gly | Arg | Pro | Glu | Leu | Pro | Pro | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| Gln | Ala | His | Gly | Leu | Gly | Val | Asp | Gly | Ala | Cys | Arg | Pro | Cys | Ser | Asp | |
| | | | 165 | | | | | 170 | | | | | | 175 | | |
| Ala | Glu | Leu | Leu | Leu | Ala | Ala | Cys | Thr | Ser | Asp | Phe | Gly | Glu | Gly | Gly | |
| | | | 180 | | | | | 185 | | | | | 190 | | | |
| Ala | His | Cys | Phe | Gly | Gly | Asp | Gly | Thr | Ile | Asn | Lys | Asn | Ser | Val | His | |
| | | 195 | | | | | 200 | | | | | 205 | | | | |
| Ala | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | Lys | |
| | 210 | | | | | 215 | | | | | | 220 | | | | |
| Lys | Gly | Gly | Arg | Lys | Lys | Asn | Thr | Pro | Glu | Gly | Gly | Pro | Lys | Lys | Ser | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| Glu | Asn | Pro | Asn | Val | Cys | Met | Val | His | Lys | Glu | Gly | Asp | Asp | Gln | Lys | |
| | | | | 245 | | | | | 250 | | | | | 255 | | |
| Glu | Arg | Asn | Gly | Asn | Ile | Lys | Ala | Asn | Gly | Arg | Lys | Glu | Arg | Thr | Val | |
| | | | 260 | | | | | 265 | | | | | 270 | | | |
| Thr | Thr | His | Arg | Ser | Lys | Ser | Glu | Lys | Lys | Val | His | Lys | Gln | Glu | Glu | |
| | | 275 | | | | | 280 | | | | | 285 | | | | |
| Thr | Ile | Gly | Glu | Arg | Asn | Thr | Asn | Asn | Gly | Gly | Gly | Glu | Arg | Asn | Ala | |
| | 290 | | | | | 295 | | | | | 300 | | | | | |
| Asn | Lys | Ser | Thr | Lys | Thr | Lys | Tyr | Tyr | Ser | Thr | Lys | Lys | Glu | Asn | Tyr | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | |

628

Met Lys Thr Arg Ile Glu Gly Gly Arg Lys Asn Ile
 325 330

<210> 482
 <211> 84
 <212> PRT
 <213> Homo sapien

<400> 482

Met Gln Gly Arg Leu Leu Pro Leu Pro Asp Ile Ser Phe Trp Ala Cys
 1 5 10 15

Ser Phe Ser Pro Thr Phe Ser Leu Thr Ser Phe Lys Ser Tyr Glu Val
 20 25 30

Pro Phe Lys Thr Ser Tyr Ser Leu Lys Pro Ser Leu Tyr Gln Phe Asp
 35 40 45

Leu Ala Ser Ile Gly Thr Glu Lys Ser Gly Asn Glu Arg Cys Asp Cys
 50 55 60

Lys Leu Ile Trp Gln Lys Glu Glu Asp Ser Cys Val Gln Lys Ser Leu
 65 70 75 80

Trp Leu Thr Glu

<210> 483
 <211> 46
 <212> PRT
 <213> Homo sapien

<400> 483

Met Cys Thr Thr Val Met Gly Pro Glu Leu Gly Pro Leu Trp Gly Glu
 1 5 10 15

Trp Thr Leu Ser Trp Gly Ser His Leu Trp Asp Thr Lys Lys Leu Ser
 20 25 30

Ser Glu His Asp Val Leu Thr Arg Tyr Val Lys Lys Ser Lys
 35 40 45

<210> 484
 <211> 65
 <212> PRT
 <213> Homo sapien

<400> 484

629

Cys Ile Asn Phe Asp Phe Leu Thr Tyr Arg Val Lys Thr Ser Cys Ser
 1 5 10 15

Leu Leu Ser Phe Leu Val Ser His Lys Trp Asp Pro Gln Leu Ser Val
 20 25 30

His Ser Pro His Ser Gly Pro Ser Ser Gly Pro Met Thr Val Val His
 35 40 45

Ile Ala Lys Glu Gln His Gly Ser Gly Pro Gln Thr Leu Pro Gln Pro
 50 55 60

Cys
 65

<210> 485
 <211> 54
 <212> PRT
 <213> Homo sapien

<400> 485

Met Ser His Ser Glu Ile Leu Ile Ser Leu Gln Arg Ala Arg Lys Lys
 1 5 10 15

Leu Pro Thr Leu His Pro Ile Phe Ser Val Cys Val Lys Ser Pro Val
 20 25 30

Lys Gln Asp Ile Ala Ala Gln Phe Arg Asn Val Lys His Val Thr Met
 35 40 45

Ile Gln Glu Leu Pro Ile
 50

<210> 486
 <211> 40
 <212> PRT
 <213> Homo sapien

<400> 486

Met Pro Thr Asn Gln Leu Leu Val Ala Pro Val Asn Thr Pro Cys Phe
 1 5 10 15

Pro Leu Glu Arg Leu Leu Tyr Cys Ile Trp Cys Gln Cys Leu Arg Lys
 20 25 30

Gln Gln Tyr Gln Pro Pro Leu His
 35 40

630

<210> 487
 <211> 50
 <212> PRT
 <213> Homo sapien

<400> 487

Met Val Val Lys His Phe Lys Asp Thr Ser Ile Leu Gly Leu Cys Ser
 1 5 10 15

Pro Glu Ser Ser Leu His Ile Phe Pro Thr Ile Gln Pro His Gln Glu
 20 25 30

Met Ile Thr Ala Gln Lys Val Tyr Gln Tyr Leu Pro Lys Leu Met Asp
 35 40 45

Leu Lys
 50

<210> 488
 <211> 60
 <212> PRT
 <213> Homo sapien

<400> 488

Met Lys Val Cys Phe Ala Ala Ala Thr Ala His Leu Leu Arg Pro Leu
 1 5 10 15

Gln Gln Arg Leu Ser Thr Ile Leu Gly Lys Leu Gly Gly Ala Lys Val
 20 25 30

His Gly Ser Ser Gly Thr Ser His Thr Arg Ile Cys Leu Met Glu Val
 35 40 45

Thr Gln Gly Gly Arg Asn Glu Gln Phe Ile Leu His
 50 55 60

<210> 489
 <211> 67
 <212> PRT
 <213> Homo sapien

<400> 489

Met Asn Arg Leu Trp Tyr Trp Phe Glu Glu Ile Lys Ser Leu Asn Gly
 1 5 10 15

Leu Lys Glu Ile Ile Leu Leu Ile Cys Gln Asn Pro Cys Phe Gln Arg
 20 25 30

631

Arg Leu Thr Thr Gly Ser Leu Trp Lys Leu Ile Ile Lys Cys Ile Leu
 35 40 45

Leu Tyr Ile Lys Pro Phe His Ala Ala Asn Thr Thr Ile Tyr Phe Cys
 50 55 60

Asn Ile Asn
 65

<210> 490
 <211> 19
 <212> PRT
 <213> Homo sapien

<400> 490

Met Phe Phe Lys Leu Leu Ser Asn Glu Cys Thr Val Lys Ser Lys Ile
 1 5 10 15

Asn Gln Val

<210> 491
 <211> 26
 <212> PRT
 <213> Homo sapien

<400> 491

Met Thr Ala Tyr Ser Ser Thr Leu Lys Thr Ser Thr Phe Phe Phe Leu
 1 5 10 15

Gly Leu Ser Glu Leu Thr Arg Thr Asn Gln
 20 25

<210> 492
 <211> 156
 <212> PRT
 <213> Homo sapien

<400> 492

Met Lys Gly Leu Asp Trp Val Asn Thr Glu Pro Pro Pro Glu Ser Glu
 1 5 10 15

Ser Leu Leu Ser Val Asp Leu Pro Asp Leu Gly Trp Leu Cys Trp Tyr
 20 25 30

Ser His Phe Leu Leu His Ile Tyr Leu Pro Leu Val Ser His Ile Val
 35 40 45

632

Ser Cys Met Ser Cys Cys Pro Arg Ala Leu Thr Gly Thr Pro Ile Ile
 50 55 60

Asn Ser Cys Pro Cys Ser Gly His Gly Gly Pro Ala Trp Leu Gly Gln
 65 70 75 80

Thr Gln Trp Pro Val Gly Ala Arg Ala Pro Pro Ser Arg Thr Gly Gln
 85 90 95

Arg Ser Gln Pro Gln Gly Gln Gly Lys Ala Ser Ala Pro Thr Val Ala
 100 105 110

Thr Ser Ser Arg Pro Ser Thr Phe Leu Arg Leu Ile Trp Arg Pro Ala
 115 120 125

Pro Leu Asp Ser Ala Leu Pro Pro Arg Lys Gln His Pro Glu Leu Arg
 130 135 140

Ala Glu Glu Leu Gln Gly Leu Gly Thr Gly Pro Ala
 145 150 155

<210> 493

<211> 156

<212> PRT

<213> Homo sapien

<400> 493

Met Lys Gly Leu Asp Trp Val Asn Thr Glu Pro Pro Pro Glu Ser Glu
 1 5 10 15

Ser Leu Leu Ser Val Asp Leu Pro Asp Leu Gly Trp Leu Cys Trp Tyr
 20 25 30

Ser His Phe Leu Leu His Ile Tyr Leu Pro Leu Val Ser His Ile Val
 35 40 45

Ser Cys Met Ser Cys Cys Pro Arg Ala Leu Thr Gly Thr Pro Ile Ile
 50 55 60

Asn Ser Cys Pro Cys Ser Gly His Gly Gly Pro Ala Trp Leu Gly Gln
 65 70 75 80

Thr Gln Trp Pro Val Gly Ala Arg Ala Pro Pro Ser Arg Thr Gly Gln
 85 90 95

Arg Ser Gln Pro Gln Gly Gln Gly Lys Ala Ser Ala Pro Thr Val Ala

633

100

105

110

Thr Ser Ser Arg Pro Ser Thr Phe Leu Arg Leu Ile Trp Arg Pro Ala
 115 120 125

Pro Leu Asp Ser Ala Leu Pro Pro Arg Lys Gln His Pro Glu Leu Arg
 130 135 140

Ala Glu Glu Leu Gln Gly Leu Gly Thr Gly Pro Ala
 145 150 155

<210> 494
 <211> 39
 <212> PRT
 <213> Homo sapien

<400> 494

Met Gln Arg Gln Val Gly Arg Thr Gly Leu Leu Trp Ser Ser Val Ser
 1 5 10 15

Leu Leu Pro Trp Pro Leu Leu Pro Leu Cys Ser Gly Leu Leu Gly Arg
 20 25 30

Gly Leu Leu Ser Lys Ala Gly
 35

<210> 495
 <211> 43
 <212> PRT
 <213> Homo sapien

<400> 495

Met Thr Asn Tyr Tyr Ser Thr Gly Ile Leu Phe Leu Ile Asp Phe Pro
 1 5 10 15

Lys Lys Leu His Val Cys Val Phe Phe Ser Val Ile His Leu Ser His
 20 25 30

Lys Met Lys Ser Ala Cys Ser His Leu Pro Gln
 35 40

<210> 496
 <211> 94
 <212> PRT
 <213> Homo sapien

<400> 496

Met Gln Lys Arg Pro Gln Ile Glu Ser Arg Cys Leu Gly Pro Leu Leu

634

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| 1 | | | | 5 | | | | | | 10 | | | | | | 15 |
| Pro | Gln | Gly | Leu | Leu | Pro | Thr | Glu | Gly | Pro | Met | Asp | His | Phe | Pro | Leu | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |
| Asn | Ala | Ser | Thr | Arg | Thr | Ala | Trp | Val | Ala | Asp | Ile | Asp | Gly | Asp | Ala | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| Gln | Ser | Ser | Trp | Pro | Arg | Trp | Gly | Thr | Glu | Pro | Gln | Ala | Val | Ala | Arg | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| Gln | Pro | Leu | Arg | Pro | Arg | Phe | Arg | Lys | Val | Pro | Leu | Leu | Pro | Arg | Arg | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| Asn | Val | Arg | Glu | Arg | Pro | Gly | Gly | Trp | Ala | Met | Leu | Val | Val | | | |
| | | | | 85 | | | | | 90 | | | | | | | |

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<210> 497
<211> 62
<212> PRT
<213> Homo sapien
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<400> 497

Met Asp Gly Gly Lys Gln Met Asn Lys Asn Gly Glu Glu Arg Gly Leu
1 5 10 15

Glu Ala Thr Ala Tyr Pro Ala Thr Ser Trp Ala Thr Thr His Arg Pro
20 25 30

Ile Leu Glu His Ile Ser Val Thr His Arg Val Asn Gly Ile Ile Pro
35 40 45

Cys Glu Leu Ser Ala Ser Leu Lys Leu His Pro Ser Ala His
50 55 60

| | |
|-------|-------------|
| <210> | 498 |
| <211> | 43 |
| <212> | PRT |
| <213> | Homo sapien |

<400> 498

Leu Asp Ser Gln Pro His Leu Trp Ser Pro Arg Pro Leu Ser His Arg
1 5 10 15

Arg Cys Tyr Gly Ser Leu Asn Glu Arg Thr Arg Asp Ser Val His His
20 25 30

635

Val Ala Leu Asp Leu Ala Leu Val Leu Arg Leu
 35 40

<210> 499
 <211> 100
 <212> PRT
 <213> Homo sapien

<400> 499

Met Glu His Asn Tyr Gln Gln Gly Val Gly Met Glu Lys Leu Lys Leu
 1 5 10 15

Pro Met Phe Phe Gln Ser Asn Asn Asn Pro Ser Leu Ala Ile Ser Trp
 20 25 30

Thr Leu Asn Val Ser Lys Tyr Asn Met Lys Lys Lys Asn Leu Ser His
 35 40 45

His Ala Gln Pro Thr Pro Trp Cys Ile Asp Leu Leu Ser Ala Ser Gly
 50 55 60

Asn Gly Cys Gly His Asn Val Val Ser Trp Glu Ser Ser Cys Ile Gln
 65 70 75 80

Gly Ile Val Met Arg Glu Arg Leu Val Asn Arg Ile Gly Val His Leu
 85 90 95

Pro Trp His Ser
 100

<210> 500
 <211> 54
 <212> PRT
 <213> Homo sapien

<400> 500

Met Met Thr Ala Ala Leu Leu Trp Trp Asp Tyr Phe Gly Gly Trp Met
 1 5 10 15

Trp Pro Arg Glu Val Cys Thr Leu Ser Gly Gln Ala Phe Cys Phe Asp
 20 25 30

His Phe Val Ala Gln His Leu Thr Gln Gly Ala Arg Asp Ser Arg Pro
 35 40 45

Tyr Val Lys Arg Glu Gly
 50

636

<210> 501
 <211> 11
 <212> PRT
 <213> Homo sapien

<400> 501

Met Val Phe Phe Ile Thr Phe Ile Val Phe Leu
 1 5 10

<210> 502
 <211> 126
 <212> PRT
 <213> Homo sapien

<400> 502

Met Thr Gly Phe Gly Asn Pro Ile Ala Ser Glu Phe Gln Gly Gly Glu
 1 5 10 15

Glu Lys Asp Ala Gly Glu Asn Leu Leu Ser Glu Gly Phe Pro Leu Ala
 20 25 30

Ala Ser Ser Thr Lys Leu Thr His Lys Leu His Val Lys Phe Pro Asn
 35 40 45

Leu His Leu Gly Glu Gln Ala Leu Ser Leu Gln Arg Ile Gln Arg His
 50 55 60

Leu Glu Gly Ile Cys Gln Gly Arg His Arg Val Arg Arg Trp Gly Trp
 65 70 75 80

Gly Phe Leu Asp Ser Ser Gly Pro Leu Gln Pro His Arg Ala Cys Asn
 85 90 95

Val Ala Asp Ala Ala Gly Glu Leu Val Ser Glu Arg Arg Met His Glu
 100 105 110

Ser Glu Leu Glu Thr Glu Gly Gln Lys Asp Gln Glu Lys Lys
 115 120 125

<210> 503
 <211> 126
 <212> PRT
 <213> Homo sapien

<400> 503

Met Thr Gly Phe Gly Asn Pro Ile Ala Ser Glu Phe Gln Gly Gly Glu
 1 5 10 15

637

Glu Lys Asp Ala Gly Glu Asn Leu Leu Ser Glu Gly Phe Pro Leu Ala
 20 25 30

Ala Ser Ser Thr Lys Leu Thr His Lys Leu His Val Lys Phe Pro Asn
 35 40 45

Leu His Leu Gly Glu Gln Ala Leu Ser Leu Gln Arg Ile Gln Arg His
 50 55 60

Leu Glu Gly Ile Cys Gln Gly Arg His Arg Val Arg Arg Trp Gly Trp
 65 70 75 80

Gly Phe Leu Asp Ser Ser Gly Pro Leu Gln Pro His Arg Ala Cys Asn
 85 90 95

Val Ala Asp Ala Ala Gly Glu Leu Val Ser Glu Arg Arg Met His Glu
 100 105 110

Ser Glu Leu Glu Thr Glu Gly Gln Lys Asp Gln Glu Lys Lys
 115 120 125

<210> 504
 <211> 10
 <212> PRT
 <213> Homo sapien

<400> 504

Met Gly Leu Phe Leu Val Glu Lys Val Leu
 1 5 10

<210> 505
 <211> 141
 <212> PRT
 <213> Homo sapien

<400> 505

Met Ser Ile Cys Arg Arg Gln Glu Asp Thr Val Trp Leu Ala Trp Ala
 1 5 10 15

Ser Leu Ala Asp Arg Gly Ala Ala Gln Pro Asp His Arg Gly Phe Met
 20 25 30

Ala Gly Thr Pro Asp His Ser Leu Ile Leu Ser Asp Phe Thr His His
 35 40 45

Leu Ala Ser Ala Gln Ser Cys His Cys Ala Phe Pro Asp Met Ser Ala
 50 55 60

638

Ala Gly Thr His Thr Arg Glu Arg Leu Leu Ser Pro Ala Lys Ser Thr
65 70 75 80

Gly Glu Lys Ala Leu Pro Pro Gly Lys Gln Arg Gln Pro Cys Ser Val
85 90 95

Thr Thr Asn Leu Tyr Lys Ala Gln Gly Leu Ile Val Asp Phe Leu Gln
100 105 110

Gln Val Ser Cys Val Arg Pro Gly Pro Leu Pro Ser Ile Leu Asn Ala
115 120 125

Arg His Leu Asn Ser Pro Ala Cys Gln Ser Gly Ile Pro
130 135 140

<210> 506

<211> 141

<212> PRT

<213> Homo sapien

<400> 506

Met Ser Ile Cys Arg Arg Gln Glu Asp Thr Val Trp Leu Ala Trp Ala
1 5 10 15

Ser Leu Ala Asp Arg Gly Ala Ala Gln Pro Asp His Arg Gly Phe Met
20 25 30

Ala Gly Thr Pro Asp His Ser Leu Ile Leu Ser Asp Phe Thr His His
35 40 45

Leu Ala Ser Ala Gln Ser Cys His Cys Ala Phe Pro Asp Met Ser Ala
50 55 60

Ala Gly Thr His Thr Arg Glu Arg Leu Leu Ser Pro Ala Lys Ser Thr
65 70 75 80

Gly Glu Lys Ala Leu Pro Pro Gly Lys Gln Arg Gln Pro Cys Ser Val
85 90 95

Thr Thr Asn Leu Tyr Lys Ala Gln Gly Leu Ile Val Asp Phe Leu Gln
100 105 110

Gln Val Ser Cys Val Arg Pro Gly Pro Leu Pro Ser Ile Leu Asn Ala
115 120 125

639

Arg His Leu Asn Ser Pro Ala Cys Gln Ser Gly Ile Pro
130 135 140

<210> 507
<211> 86
<212> PRT
<213> Homo sapien

<400> 507

Met Tyr Leu Asn Gln Cys Arg Asn Gln Gly Asn Ile Cys Asp Glu Met
1 5 10 15

Gln Arg Arg Asn Cys Leu His Leu Gly Cys Arg Cys Met Ala Met Ala
20 25 30

Lys Ala Asp Gly Phe Pro Arg Ser Ser Gln Leu Cys Gln Ala Val Glu
35 40 45

Ala Thr Val Leu Ala Gly Ala Val Pro Gly Val Gly Ser Lys Ala Pro
50 55 60

Pro Ser Asp Gly Leu Ile Glu Thr Arg Leu Gly Tyr Phe Trp Asp Ser
65 70 75 80

Ser Leu Pro Ala Pro Leu
85

<210> 508
<211> 32
<212> PRT
<213> Homo sapien

<400> 508

Met Lys Tyr Leu Ala Asp Gly Ser Leu Leu Lys Pro Asp Glu Leu Glu
1 5 10 15

Ser Ser Asp Phe Asn Cys Leu Trp Val Leu Arg Val Lys Ser Leu Arg
20 25 30

<210> 509
<211> 33
<212> PRT
<213> Homo sapien

<400> 509

Met Lys Tyr Leu Ala Asp Gly Ser Leu Leu Lys Pro Asp Glu Leu Glu
1 5 10 15

640

Ser Ser Asp Phe Val Cys Leu Phe Ser Asp Arg Val Thr Asn His Ser
 20 25 30

Gly

<210> 510
 <211> 42
 <212> PRT
 <213> Homo sapien

<400> 510

Met Val Pro Gln Gln Thr Gly Leu Gly Ile Gly Arg His Thr Ala Met
 1 5 10 15

Ile Cys His Leu Lys His Leu Trp Ser Asp Ser Val Gly Lys Leu Leu
 20 25 30

Thr Phe Leu Lys Asn Val Leu Thr Phe Lys
 35 40

<210> 511
 <211> 47
 <212> PRT
 <213> Homo sapien

<400> 511

Met His Leu Lys Leu Ser Leu Arg His Gln Gln Leu Leu Trp Ala Lys
 1 5 10 15

Arg Asn Cys Pro Asp Arg Lys Lys His Phe Trp Val Leu Val Lys His
 20 25 30

Cys Leu Asn Ile Trp Ile Leu Leu Phe Ser Leu Leu Leu Gln Glu
 35 40 45

<210> 512
 <211> 30
 <212> PRT
 <213> Homo sapien

<400> 512

Met Lys Lys Ser Phe Cys Thr Tyr Thr Asn Val Glu Tyr Tyr Val Ala
 1 5 10 15

Val Leu Asn Phe Lys Asn Gln Met Gln Lys Ile Ser Val Tyr
 20 25 30

641

<210> 513
 <211> 21
 <212> PRT
 <213> Homo sapien

<400> 513

Met Phe Gln Arg Phe Ser Pro Val Phe Ser Ser Lys Ser Leu Met Gly
 1 5 10 15

Leu Phe Phe Phe Phe
 20

<210> 514
 <211> 144
 <212> PRT
 <213> Homo sapien

<400> 514

Met Leu Ile Pro Lys Ser Pro Pro Gly Ala Leu Ser Asp His Lys Ser
 1 5 10 15

Pro Thr Ser Ser Pro Pro Ala Ala Thr Trp Lys Pro Ala Phe Pro Pro
 20 25 30

Ala Gln His Leu Gln Ala Ser Pro Gly Gln Pro Ala Gln Val His Val
 35 40 45

Leu Pro Phe Pro Pro Asp Pro Thr Ser Ser Pro Pro Arg Gln Ser Pro
 50 55 60

Ile Pro Gly Gln Ser Arg Arg Gln Leu Arg Pro Cys Lys Trp Leu Lys
 65 70 75 80

Asp Pro Val Trp Cys His Gly Leu Asp Trp Ser Arg Ser Gln Thr Val
 85 90 95

Ile Ser Asn Pro Lys Leu Gly Asn Phe Met Pro Leu Phe Ser Pro Glu
 100 105 110

Pro Ala Leu Thr Ala Thr Pro Cys Gly Val Leu Gly Pro Trp Pro Phe
 115 120 125

Thr Leu Ser Gln Glu Gly Pro Cys Cys Arg Pro Trp Pro Ser Gly Ser
 130 135 140

<210> 515
 <211> 966
 <212> PRT

642

<213> Homo sapien

<400> 515

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro

643

| | | | | | | |
|---|-----|-----|-----|-----|-----|-----|
| 225 | | 230 | | 235 | | 240 |
| Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His | | | | | | |
| | 245 | | 250 | | 255 | |
| Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val | | | | | | |
| | 260 | | 265 | | 270 | |
| Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg | | | | | | |
| | 275 | | 280 | | 285 | |
| His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser | | | | | | |
| | 290 | | 295 | | 300 | |
| Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly | | | | | | |
| 305 | | 310 | | 315 | | 320 |
| Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn | | | | | | |
| | 325 | | 330 | | 335 | |
| Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser | | | | | | |
| | 340 | | 345 | | 350 | |
| Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg | | | | | | |
| | 355 | | 360 | | 365 | |
| His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg | | | | | | |
| | 370 | | 375 | | 380 | |
| Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys | | | | | | |
| 385 | | 390 | | 395 | | 400 |
| Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg | | | | | | |
| | 405 | | 410 | | 415 | |
| Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala | | | | | | |
| | 420 | | 425 | | 430 | |
| Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro | | | | | | |
| | 435 | | 440 | | 445 | |
| Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys | | | | | | |
| | 450 | | 455 | | 460 | |
| Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu | | | | | | |
| 465 | | 470 | | 475 | | 480 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Gln | Ala | Glu | Asp | Arg | Asp | Asp | Met | Leu | Gly | Trp | Ile | Arg | Ala | Ile |
| | | | Ser | 485 | | | | | 490 | | | | | 495 | |
| Arg | Glu | Asn | Ser | 500 | Arg | Ala | Glu | Gly | Glu | Asp | Pro | Gly | Cys | Ala | Asn |
| | | | | | | | | | 505 | | | | | 510 | Gln |
| Ala | Leu | Ile | Ser | 515 | Lys | Lys | Leu | Asn | Asp | Tyr | Arg | Lys | Val | Ser | His |
| | | | | | | | | 520 | | | | | 525 | | Ser |
| Ser | Gly | Pro | Lys | 530 | Ala | Asp | Ser | Ser | Pro | Lys | Gly | Ser | Arg | Gly | Leu |
| | | | | | | | 535 | | | | | 540 | | | Gly |
| Gly | Leu | Lys | Ser | 545 | Glu | Phe | Leu | Lys | Gln | Ser | Ala | Ala | Arg | Gly | Leu |
| | | | | | | 550 | | | | | 555 | | | | Arg |
| Thr | Gln | Asp | Leu | 565 | Pro | Ala | Gly | Ser | Lys | Asp | Asp | Ser | Ala | Ala | Ala |
| | | | | | | | | | | 570 | | | | | Pro |
| Lys | Thr | Pro | Trp | 580 | Gly | Ile | Asn | Ile | Ile | Lys | Lys | Asn | Lys | Lys | Ala |
| | | | | | | | | 585 | | | | | 590 | | Ala |
| Pro | Arg | Ala | Phe | 595 | Gly | Val | Arg | Leu | Glu | Glu | Cys | Gln | Pro | Ala | Thr |
| | | | | | | | | 600 | | | | | 605 | | Glu |
| Asn | Gln | Arg | Val | 610 | Pro | Leu | Ile | Val | Ala | Ala | Cys | Cys | Arg | Ile | Val |
| | | | | | | | 615 | | | | | 620 | | | Glu |
| Ala | Arg | Gly | Leu | 625 | Glu | Ser | Thr | Gly | Ile | Tyr | Arg | Val | Pro | Gly | Asn |
| | | | | | | 630 | | | | | 635 | | | | Asn |
| Ala | Val | Val | Ser | 645 | Ser | Leu | Gln | Glu | Gln | Leu | Asn | Arg | Gly | Pro | Gly |
| | | | | | | | | | | 650 | | | | | Asp |
| Ile | Asn | Leu | Gln | 660 | Asp | Glu | Arg | Trp | Gln | Asp | Leu | Asn | Val | Ile | Ser |
| | | | | | | | | | 665 | | | | | 670 | Ser |
| Leu | Leu | Lys | Ser | 675 | Phe | Phe | Arg | Lys | Leu | Pro | Glu | Pro | Leu | Phe | Thr |
| | | | | | | | | 680 | | | | | 685 | | Asp |
| Asp | Lys | Tyr | Asn | 690 | Asp | Phe | Ile | Glu | Ala | Asn | Arg | Ile | Glu | Asp | Ala |
| | | | | | | | 695 | | | | | 700 | | | Arg |
| Glu | Arg | Met | Arg | 705 | Thr | Leu | Arg | Lys | Leu | Ile | Arg | Asp | Leu | Pro | Gly |
| | | | | | | 710 | | | | | 715 | | | | His |

645

Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala
 725 730 735

Asp His Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val
 740 745 750

Phe Gly Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met
 755 760 765

Val Thr His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln
 770 775 780

His Ser Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr
 785 790 795 800

Pro Val Gly Asp Lys Glu Pro Gln Ala Val Pro Asn Ile Glu Tyr Leu
 805 810 815

Leu Pro Asn Ile Gly Arg Thr Val Pro Pro Gly Asp Pro Gly Ser Ala
 820 825 830

Asp Leu Leu Glu Ile Val Lys Asp Ser Thr Thr Cys Ser Ser Ala Lys
 835 840 845

Ser Lys Gly Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu Met
 850 855 860

Leu Ala Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys Arg
 865 870 875 880

Arg Glu Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu Gln
 885 890 895

Glu Ala His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln Glu
 900 905 910

Arg Pro Pro Gly Ser Arg Gly Pro Ala Ala Ala Ala Asp Ala Pro Arg
 915 920 925

Arg Arg His Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala Gly
 930 935 940

Gly Ala Ala Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile Gln
 945 950 955 960

646

Pro Val Thr Met Asp Arg
965

<210> 516
<211> 202
<212> PRT
<213> Homo sapien

<400> 516

Asp Leu Pro Gly Pro Phe Tyr Glu Arg Ser Asn Ser Leu Trp Asp Pro
1 5 10 15

Phe Ser Asp Leu Arg Leu Pro Phe Ile Ser Ser Cys Gly Ala Ala Ala
20 25 30

Thr Leu Ser Arg Ser Phe Ser Ser Pro Lys Asn Lys Lys Ala Ala Pro
35 40 45

Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu Asn
50 55 60

Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu Ala
65 70 75 80

Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn Ala
85 90 95

Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp Ile
100 105 110

Asn Leu Gln Asp Glu Arg Trp Gln Asp Leu Asn Val Ile Ser Ser Leu
115 120 125

Leu Lys Ser Phe Phe Arg Lys Leu Pro Glu Pro Leu Phe Thr Asp Asp
130 135 140

Lys Tyr Asn Asp Phe Ile Glu Ala Asn Arg Ile Glu Asp Ala Arg Glu
145 150 155 160

Arg Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His Tyr
165 170 175

Tyr Glu Thr Leu Lys Phe Leu Val Gly Pro Phe Leu Arg Gln Arg Leu
180 185 190

Pro Phe Ile Ser Ser Cys Gly Asp Ala Ala
195 200

647

<210> 517
 <211> 103
 <212> PRT
 <213> Homo sapien

<400> 517

Met Leu Ala Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys
 1 5 10 15

Arg Arg Glu Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu
 20 25 30

Gln Glu Ala His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln
 35 40 45

Glu Arg Pro Pro Gly Ser Arg Gly Pro Ala Ala Ala Ala Asp Ala Pro
 50 55 60

Arg Arg Arg His Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala
 65 70 75 80

Gly Gly Ala Ala Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile
 85 90 95

Gln Pro Val Thr Met Asp Arg
 100

<210> 518
 <211> 958
 <212> PRT
 <213> Homo sapien

<400> 518

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala

648

| | | | | | | |
|---|-----|-----|-----|-----|-----|-----|
| 65 | | 70 | | 75 | | 80 |
| Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro | | | | | | |
| | 85 | | 90 | | 95 | |
| Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr | | | | | | |
| | 100 | | 105 | | 110 | |
| Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala | | | | | | |
| | 115 | | 120 | | 125 | |
| Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu | | | | | | |
| | 130 | | 135 | | 140 | |
| Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg | | | | | | |
| | 145 | | 150 | | 155 | 160 |
| Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu | | | | | | |
| | | 165 | | 170 | | 175 |
| Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg | | | | | | |
| | 180 | | 185 | | 190 | |
| Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp | | | | | | |
| | 195 | | 200 | | 205 | |
| Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg | | | | | | |
| | 210 | | 215 | | 220 | |
| Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro | | | | | | |
| | 225 | | 230 | | 235 | 240 |
| Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His | | | | | | |
| | 245 | | 250 | | 255 | |
| Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val | | | | | | |
| | 260 | | 265 | | 270 | |
| Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg | | | | | | |
| | 275 | | 280 | | 285 | |
| His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser | | | | | | |
| | 290 | | 295 | | 300 | |
| Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly | | | | | | |
| | 305 | | 310 | | 315 | 320 |

649

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser
340 345 350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
355 360 365

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
370 375 380

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
420 425 430

Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro
435 440 445

Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys
450 455 460

Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu
465 470 475 480

Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile
485 490 495

Arg Glu Asn Ser Arg Ala Glu Gly Glu Asp Pro Gly Cys Ala Asn Gln
500 505 510

Ala Leu Ile Ser Lys Lys Leu Asn Asp Tyr Arg Lys Val Ser His Ser
515 520 525

Ser Gly Pro Lys Ala Asp Ser Ser Pro Lys Gly Ser Arg Gly Leu Gly
530 535 540

Gly Leu Lys Ser Glu Phe Leu Lys Gln Ser Ala Ala Arg Gly Leu Arg
545 550 555 560

650

Thr Gln Asp Leu Pro Ala Gly Ser Lys Asp Asp Ser Ala Ala Ala Pro
 565 570 575

Lys Thr Pro Trp Gly Ile Asn Ile Ile Lys Lys Asn Lys Lys Ala Ala
 580 585 590

Pro Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu
 595 600 605

Asn Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu
 610 615 620

Ala Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn
 625 630 635 640

Ala Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp
 645 650 655

Ile Asn Leu Gln Asp Glu Arg Trp Gln Asp Leu Asn Val Ile Ser Ser
 660 665 670

Leu Leu Lys Ser Phe Phe Arg Lys Leu Pro Glu Pro Leu Phe Thr Asp
 675 680 685

Asp Lys Tyr Asn Asp Phe Ile Glu Ala Asn Arg Ile Glu Asp Ala Arg
 690 695 700

Glu Arg Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His
 705 710 715 720

Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala
 725 730 735

Asp His Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val
 740 745 750

Phe Gly Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met
 755 760 765

Val Thr His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln
 770 775 780

His Ser Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr
 785 790 795 800

651

Pro Val Gly Asp Lys Glu Pro Gln Ala Val Pro Asn Ile Glu Tyr Leu
 805 810 815

Leu Pro Asn Ile Gly Arg Thr Val Pro Pro Gly Asp Pro Gly Ser Asp
 820 825 830

Ser Thr Thr Cys Ser Ser Ala Lys Ser Lys Gly Ser Trp Ala Pro Lys
 835 840 845

Lys Glu Pro Tyr Ala Arg Glu Met Leu Ala Ile Ser Phe Ile Ser Ala
 850 855 860

Val Asn Arg Lys Arg Lys Lys Arg Arg Glu Ala Arg Gly Leu Gly Ser
 865 870 875 880

Ser Thr Asp Asp Asp Ser Glu Gln Glu Ala His Lys Pro Gly Ala Gly
 885 890 895

Ala Thr Ala Pro Gly Thr Gln Glu Arg Pro Pro Gly Ser Arg Gly Pro
 900 905 910

Ala Ala Ala Ala Asp Ala Pro Arg Arg Arg His Arg Gly Pro Arg Thr
 915 920 925

Arg Gln Ser Pro Gly Gly Ala Gly Gly Ala Ala Gly Arg Gly Asp Ala
 930 935 940

Leu His Cys Val Gly Leu Ile Gln Pro Val Thr Met Asp Arg
 945 950 955

<210> 519
 <211> 837
 <212> PRT
 <213> Homo sapien

<400> 519

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

652

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

653

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser
 340 345 350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
 355 360 365

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
 370 375 380

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
 385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
 405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
 420 425 430

Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro
 435 440 445

Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys
 450 455 460

Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu
 465 470 475 480

Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile
 485 490 495

Arg Glu Asn Ser Arg Ala Glu Gly Glu Asp Pro Gly Cys Ala Asn Gln
 500 505 510

Ala Leu Ile Ser Lys Lys Leu Asn Asp Tyr Arg Lys Val Ser His Ser
 515 520 525

Ser Gly Pro Lys Ala Asp Ser Ser Pro Lys Gly Ser Arg Gly Leu Gly
 530 535 540

654

Gly Leu Lys Ser Glu Phe Leu Lys Gln Ser Ala Ala Arg Gly Leu Arg
 545 550 555 560

Thr Gln Asp Leu Pro Ala Gly Ser Lys Asp Asp Ser Ala Ala Ala Pro
 565 570 575

Lys Thr Pro Trp Gly Ile Asn Ile Ile Lys Lys Asn Lys Lys Ala Ala
 580 585 590

Pro Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu
 595 600 605

Asn Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu
 610 615 620

Ala Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn
 625 630 635 640

Ala Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp
 645 650 655

Ile Asn Leu Gln Asp Glu Arg Trp Gln Asp Leu Asn Val Ile Ser Ser
 660 665 670

Leu Leu Lys Ser Phe Phe Arg Lys Leu Pro Glu Pro Leu Phe Thr Asp
 675 680 685

Asp Lys Tyr Asn Asp Phe Ile Glu Ala Asn Arg Ile Glu Asp Ala Arg
 690 695 700

Glu Arg Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His
 705 710 715 720

Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala
 725 730 735

Asp His Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val
 740 745 750

Phe Gly Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met
 755 760 765

Val Thr His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln
 770 775 780

His Ser Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr

| | | | | | | | | | | | | | | | | | | | | | | |
|-------|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|--|-----|
| 785 | | | | | | 790 | | | | | | | | | | 795 | | | | | | 800 |
| Pro | Val | Gly | Asp | Lys | Glu | Pro | Gln | Ala | Val | Pro | Asn | Ile | Glu | Tyr | Leu | | | | | | | |
| | | | | 805 | | | | | 810 | | | | | 815 | | | | | | | | |
| Leu | Pro | Asn | Ile | Gly | Arg | Thr | Val | Pro | Pro | Gly | Asp | Pro | Gly | Ser | Ala | | | | | | | |
| | | | 820 | | | | | 825 | | | | | 830 | | | | | | | | | |
| Asp | Leu | Leu | Glu | Ile | | | | | | | | | | | | | | | | | | |
| | | | 835 | | | | | | | | | | | | | | | | | | | |
| <210> | 520 | | | | | | | | | | | | | | | | | | | | | |
| <211> | 470 | | | | | | | | | | | | | | | | | | | | | |
| <212> | PRT | | | | | | | | | | | | | | | | | | | | | |
| <213> | Homo sapien | | | | | | | | | | | | | | | | | | | | | |
| <400> | 520 | | | | | | | | | | | | | | | | | | | | | |
| Met | Leu | Gly | Trp | Ile | Arg | Ala | Ile | Arg | Glu | Asn | Ser | Arg | Ala | Glu | Gly | | | | | | | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | | | | | | | |
| Glu | Asp | Pro | Gly | Cys | Ala | Asn | Gln | Ala | Leu | Ile | Ser | Lys | Lys | Leu | Asn | | | | | | | |
| | | | 20 | | | | | 25 | | | | | 30 | | | | | | | | | |
| Asp | Tyr | Arg | Lys | Val | Ser | His | Ser | Ser | Gly | Pro | Lys | Ala | Asp | Ser | Ser | | | | | | | |
| | | 35 | | | | | 40 | | | | | 45 | | | | | | | | | | |
| Pro | Lys | Gly | Ser | Arg | Gly | Leu | Gly | Gly | Leu | Lys | Ser | Glu | Phe | Leu | Lys | | | | | | | |
| | 50 | | | | | 55 | | | | | 60 | | | | | | | | | | | |
| Gln | Ser | Ala | Ala | Arg | Gly | Leu | Arg | Thr | Gln | Asp | Leu | Pro | Ala | Gly | Ser | | | | | | | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | | | | | | | |
| Lys | Asp | Asp | Ser | Ala | Ala | Ala | Pro | Lys | Thr | Pro | Trp | Gly | Ile | Asn | Ile | | | | | | | |
| | | | | 85 | | | | | 90 | | | | | 95 | | | | | | | | |
| Ile | Lys | Lys | Asn | Lys | Lys | Ala | Ala | Pro | Arg | Ala | Phe | Gly | Val | Arg | Leu | | | | | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | | | | | | |
| Glu | Glu | Cys | Gln | Pro | Ala | Thr | Glu | Asn | Gln | Arg | Val | Pro | Leu | Ile | Val | | | | | | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | | | | | | |
| Ala | Ala | Cys | Cys | Arg | Ile | Val | Glu | Ala | Arg | Gly | Leu | Glu | Ser | Thr | Gly | | | | | | | |
| | | 130 | | | | 135 | | | | | 140 | | | | | | | | | | | |
| Ile | Tyr | Arg | Val | Pro | Gly | Asn | Asn | Ala | Val | Val | Ser | Ser | Leu | Gln | Glu | | | | | | | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | | | | | | | |

656

Gln Leu Asn Arg Gly Pro Gly Asp Ile Asn Leu Gln Asp Glu Arg Trp
 165 170 175

Gln Asp Leu Asn Val Ile Ser Ser Leu Leu Lys Ser Phe Phe Arg Lys
 180 185 190

Leu Pro Glu Pro Leu Phe Thr Asp Asp Lys Tyr Asn Asp Phe Ile Glu
 195 200 205

Ala Asn Arg Ile Glu Asp Ala Arg Glu Arg Met Arg Thr Leu Arg Lys
 210 215 220

Leu Ile Arg Asp Leu Pro Gly His Tyr Tyr Glu Thr Leu Lys Phe Leu
 225 230 235 240

Val Gly His Leu Lys Thr Ile Ala Asp His Ser Glu Lys Asn Lys Met
 245 250 255

Glu Pro Arg Asn Leu Ala Leu Val Phe Gly Pro Thr Leu Val Arg Thr
 260 265 270

Ser Glu Asp Asn Met Thr Asp Met Val Thr His Met Pro Asp Arg Tyr
 275 280 285

Lys Ile Val Glu Thr Leu Ile Gln His Ser Asp Trp Phe Phe Ser Asp
 290 295 300

Glu Glu Asp Lys Gly Glu Arg Thr Pro Val Gly Asp Lys Glu Pro Gln
 305 310 315 320

Ala Val Pro Asn Ile Glu Tyr Leu Leu Pro Asn Ile Gly Arg Thr Val
 325 330 335

Pro Pro Gly Asp Pro Gly Ser Asp Ser Thr Thr Cys Ser Ser Ala Lys
 340 345 350

Ser Lys Gly Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu Met
 355 360 365

Leu Ala Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys Arg
 370 375 380

Arg Glu Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu Gln
 385 390 395 400

657

Glu Ala His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln Glu
 405 410 415

Arg Pro Pro Gly Ser Arg Gly Pro Ala Ala Ala Ala Asp Ala Pro Arg
 420 425 430

Arg Arg His Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala Gly
 435 440 445

Gly Ala Ala Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile Gln
 450 455 460

Pro Val Thr Met Asp Arg
 465 470

<210> 521
 <211> 252
 <212> PRT
 <213> Homo sapien

<400> 521

Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His Tyr Tyr
 1 5 10 15

Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala Asp His
 20 25 30

Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val Phe Gly
 35 40 45

Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met Val Thr
 50 55 60

His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln His Ser
 65 70 75 80

Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr Pro Val
 85 90 95

Gly Asp Lys Glu Pro Gln Ala Val Pro Asn Ile Glu Tyr Leu Leu Pro
 100 105 110

Asn Ile Gly Arg Thr Val Pro Pro Gly Asp Pro Gly Ser Asp Ser Thr
 115 120 125

Thr Cys Ser Ser Ala Lys Ser Lys Gly Ser Trp Ala Pro Lys Lys Glu
 130 135 140

658

Pro Tyr Ala Arg Glu Met Leu Ala Ile Ser Phe Ile Ser Ala Val Asn
 145 150 155 160

Arg Lys Arg Lys Lys Arg Arg Glu Ala Arg Gly Leu Gly Ser Ser Thr
 165 170 175

Asp Asp Asp Ser Glu Gln Glu Ala His Lys Pro Gly Ala Gly Ala Thr
 180 185 190

Ala Pro Gly Thr Gln Glu Arg Pro Pro Gly Ser Arg Gly Pro Ala Ala
 195 200 205

Ala Ala Asp Ala Pro Arg Arg Arg His Arg Gly Pro Arg Thr Arg Gln
 210 215 220

Ser Pro Gly Gly Ala Gly Gly Ala Ala Gly Arg Gly Asp Ala Leu His
 225 230 235 240

Cys Val Gly Leu Ile Gln Pro Val Thr Met Asp Arg
 245 250

<210> 522
 <211> 693
 <212> PRT
 <213> Homo sapien

<400> 522

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

659

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser

660

340

345

350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
 355 360 365

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
 370 375 380

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
 385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
 405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
 420 425 430

Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro
 435 440 445

Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys
 450 455 460

Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu
 465 470 475 480

Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile
 485 490 495

Arg Glu Asn Ser Arg Ala Glu Gly Glu Asp Pro Gly Cys Ala Asn Gln
 500 505 510

Ala Leu Ile Ser Lys Lys Leu Asn Asp Tyr Arg Lys Val Ser His Ser
 515 520 525

Ser Gly Pro Lys Ala Asp Ser Ser Pro Lys Gly Ser Arg Gly Leu Gly
 530 535 540

Gly Leu Lys Ser Glu Phe Leu Lys Gln Ser Ala Ala Arg Gly Leu Arg
 545 550 555 560

Thr Gln Asp Leu Pro Ala Gly Ser Lys Asp Asp Ser Ala Ala Ala Pro
 565 570 575

Lys Thr Pro Trp Gly Ile Asn Ile Ile Lys Lys Asn Lys Lys Ala Ala
 580 585 590

661

Pro Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu
 595 600 605

Asn Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu
 610 615 620

Ala Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn
 625 630 635 640

Ala Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp
 645 650 655

Ile Asn Leu Gln Asp Glu Arg Trp Gln Asp Leu Asn Val Ile Ser Ser
 660 665 670

Leu Leu Lys Ser Phe Phe Arg Lys Leu Pro Glu Pro Leu Phe Thr Asp
 675 680 685

Gly Ala Leu Leu Phe
 690

<210> 523
 <211> 697
 <212> PRT
 <213> Homo sapien

<400> 523

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

662

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser

663

| | | |
|---|-----|-----|
| 340 | 345 | 350 |
| Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg | | |
| 355 | 360 | 365 |
| His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg | | |
| 370 | 375 | 380 |
| Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys | | |
| 385 | 390 | 400 |
| Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg | | |
| 405 | 410 | 415 |
| Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala | | |
| 420 | 425 | 430 |
| Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro | | |
| 435 | 440 | 445 |
| Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys | | |
| 450 | 455 | 460 |
| Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu | | |
| 465 | 470 | 475 |
| Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile | | |
| 485 | 490 | 495 |
| Arg Glu Asn Ser Arg Ala Glu Gly Glu Asp Pro Gly Cys Ala Asn Gln | | |
| 500 | 505 | 510 |
| Ala Leu Ile Ser Lys Lys Leu Asn Asp Tyr Arg Lys Val Ser His Ser | | |
| 515 | 520 | 525 |
| Ser Gly Pro Lys Ala Asp Ser Ser Pro Lys Gly Ser Arg Gly Leu Gly | | |
| 530 | 535 | 540 |
| Gly Leu Lys Ser Glu Phe Leu Lys Gln Ser Ala Ala Arg Gly Leu Arg | | |
| 545 | 550 | 555 |
| Thr Gln Asp Leu Pro Ala Gly Ser Lys Asp Asp Ser Ala Ala Ala Pro | | |
| 565 | 570 | 575 |
| Lys Thr Pro Trp Gly Ile Asn Ile Ile Lys Lys Asn Lys Lys Ala Ala | | |
| 580 | 585 | 590 |

664

Pro Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu
595 600 605

Asn Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu
610 615 620

Ala Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn
625 630 635 640

Ala Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp
645 650 655

Ile Asn Leu Gln Asp Glu Val Gly Glu Ala Gly Gly Ser Val Glu Gly
660 665 670

Gly Leu Arg Trp Cys Val Gly Gly Ala Pro Leu Gly Glu Phe Cys Gly
675 680 685

Leu Leu Cys Cys Met His Cys Ala Leu
690 695

<210> 524

<211> 252

<212> PRT

<213> Homo sapien

<400> 524

Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His Tyr Tyr
1 5 10 15

Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala Asp His
20 25 30

Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val Phe Gly
35 40 45

Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met Val Thr
50 55 60

His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln His Ser
65 70 75 80

Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr Pro Val
85 90 95

665

Gly Asp Lys Glu Pro Gln Ala Val Pro Asn Ile Glu Tyr Leu Leu Pro
 100 105 110

Asn Ile Gly Arg Thr Val Pro Pro Gly Asp Pro Gly Ser Asp Ser Thr
 115 120 125

Thr Cys Ser Ser Ala Lys Ser Lys Gly Ser Trp Ala Pro Lys Lys Glu
 130 135 140

Pro Tyr Ala Arg Glu Met Leu Ala Ile Ser Phe Ile Ser Ala Val Asn
 145 150 155 160

Arg Lys Arg Lys Lys Arg Arg Glu Ala Arg Gly Leu Gly Ser Ser Thr
 165 170 175

Asp Asp Asp Ser Glu Gln Glu Ala His Lys Pro Gly Ala Gly Ala Thr
 180 185 190

Ala Pro Gly Thr Gln Glu Arg Pro Pro Gly Ser Arg Gly Pro Ala Ala
 195 200 205

Ala Ala Asp Ala Pro Arg Arg Arg His Arg Gly Pro Arg Thr Arg Gln
 210 215 220

Ser Pro Gly Gly Ala Gly Gly Ala Ala Gly Arg Gly Asp Ala Leu His
 225 230 235 240

Cys Val Gly Leu Ile Gln Pro Val Thr Met Asp Arg
 245 250

<210> 525

<211> 568

<212> PRT

<213> Homo sapien

<400> 525

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

666

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

667

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser
 340 345 350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
 355 360 365

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
 370 375 380

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
 385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
 405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
 420 425 430

Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro
 435 440 445

Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys
 450 455 460

Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu
 465 470 475 480

Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile
 485 490 495

Arg Glu Asn Ser Arg Ala Glu Gly Glu Val Arg Ala Arg Pro Ala Arg
 500 505 510

Gln Pro Gln Arg Ala Gly Gly Val Ala Ser His Arg Leu Trp Thr Trp
 515 520 525

Asp Ala Arg Ser Glu Pro His Phe Pro Leu Leu Glu Arg Gly Ala Asp
 530 535 540

668

Arg Ser Ala Pro Arg Asp Cys Val Pro Gln Gly Phe Gly Val Arg Arg
 545 550 555 560

Val His Arg Gln Gly Ser Arg Gly
 565

<210> 526
 <211> 260
 <212> PRT
 <213> Homo sapien

<400> 526

Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His Tyr Tyr
 1 5 10 15

Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala Asp His
 20 25 30

Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val Phe Gly
 35 40 45

Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met Val Thr
 50 55 60

His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln His Ser
 65 70 75 80

Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr Pro Val
 85 90 95

Gly Asp Lys Glu Pro Gln Ala Val Pro Asn Ile Glu Tyr Leu Leu Pro
 100 105 110

Asn Ile Gly Arg Thr Val Pro Pro Gly Asp Pro Gly Ser Ala Asp Leu
 115 120 125

Leu Glu Asp Leu Lys Asp Ser Thr Thr Cys Ser Ser Ala Lys Ser Lys
 130 135 140

Gly Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu Met Leu Ala
 145 150 155 160

Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys Arg Arg Glu
 165 170 175

Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu Gln Glu Ala
 180 185 190

669

His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln Glu Arg Pro
 195 200 205

Pro Gly Ser Arg Gly Pro Ala Ala Ala Ala Asp Ala Pro Arg Arg Arg
 210 215 220

His Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala Gly Gly Ala
 225 230 235 240

Ala Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile Gln Pro Val
 245 250 255

Thr Met Asp Arg
 260

<210> 527
 <211> 125
 <212> PRT
 <213> Homo sapien

<400> 527

Met Leu Gly Trp Ile Arg Ala Ile Arg Glu Asn Ser Arg Ala Glu Gly
 1 5 10 15

Glu Asp Pro Gly Cys Ala Asn Gln Ala Leu Ile Ser Lys Lys Leu Asn
 20 25 30

Asp Tyr Arg Lys Val Ser His Ser Ser Gly Pro Lys Ala Asp Ser Ser
 35 40 45

Pro Lys Gly Ser Arg Gly Leu Gly Gly Leu Lys Ser Glu Phe Leu Lys
 50 55 60

Gln Ser Ala Ala Arg Gly Leu Arg Thr Gln Asp Leu Pro Ala Gly Ser
 65 70 75 80

Lys Asp Asp Ser Ala Ala Ala Pro Lys Thr Pro Trp Gly Ile Asn Ile
 85 90 95

Ile Lys Lys Asn Lys Lys Ala Ala Pro Arg Ala Phe Gly Val Arg Leu
 100 105 110

Glu Glu Cys Gln Pro Ala Thr Glu Asn Gln Arg Val Pro
 115 120 125

670

<210> 528
 <211> 225
 <212> PRT
 <213> Homo sapien

<220>
 <221> MISC_FEATURE
 <222> (132)..(132)
 <223> x= any amino acid

<220>
 <221> MISC_FEATURE
 <222> (140)..(140)
 <223> x= any amino acid

<220>
 <221> MISC_FEATURE
 <222> (153)..(153)
 <223> x= any amino acid

<400> 528

Asp Leu Pro Gly Pro Phe Tyr Glu Arg Ser Asn Ser Leu Trp Asp Pro
 1 5 10 15

Phe Ser Asp Leu Arg Leu Pro Phe Ile Ser Ser Cys Gly Ala Ala Ala
 20 25 30

Thr Leu Ser Arg Ser Phe Ser Ser Pro Lys Asn Lys Lys Ala Ala Pro
 35 40 45

Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu Asn
 50 55 60

Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu Ala
 65 70 75 80

Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn Ala
 85 90 95

Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp Ile
 100 105 110

Asn Leu Gln Asp Glu Arg His Ser Ala Thr Glu Arg Val Ile Leu Leu
 115 120 125

Glu Ser Arg Xaa Ala Leu Leu Tyr Asn Gly Ala Xaa Ser Leu Arg Cys
 130 135 140

671

Lys Cys Arg Ser Thr His Glu Ser Xaa Ser Leu Tyr Gln Ala Val Asp
 145 150 155 160

Asp Leu Arg Leu Ile Thr Glu His Ser Ile Asp Gly Pro Ser Pro His
 165 170 175

Ser Asp Gly Leu Arg Val Glu Gln Asn Glu Glu Leu Arg Lys Leu Ile
 180 185 190

Arg Asp Leu Pro Gly His Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly
 195 200 205

Pro Phe Leu Arg Gln Arg Leu Pro Phe Ile Ser Ser Cys Gly Ala Ala
 210 215 220

Ala
 225

<210> 529
 <211> 917
 <212> PRT
 <213> Homo sapien

<400> 529

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

672

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser
 340 345 350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
 355 360 365

673

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
 370 375 380

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
 385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
 405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
 420 425 430

Ala Ala Gly Ala Ala Gly Pro Ala Gln Ala Glu Asp Arg Asp Asp Met
 435 440 445

Leu Gly Trp Ile Arg Ala Ile Arg Glu Asn Ser Arg Ala Glu Gly Glu
 450 455 460

Asp Pro Gly Cys Ala Asn Gln Ala Leu Ile Ser Lys Lys Leu Asn Asp
 465 470 475 480

Tyr Arg Lys Val Ser His Ser Ser Gly Pro Lys Ala Asp Ser Ser Pro
 485 490 495

Lys Gly Ser Arg Gly Leu Gly Gly Leu Lys Ser Glu Phe Leu Lys Gln
 500 505 510

Ser Ala Ala Arg Gly Leu Arg Thr Gln Asp Leu Pro Ala Gly Ser Lys
 515 520 525

Asp Asp Ser Ala Ala Ala Pro Lys Thr Pro Trp Gly Ile Asn Ile Ile
 530 535 540

Lys Lys Asn Lys Lys Ala Ala Pro Arg Ala Phe Gly Val Arg Leu Glu
 545 550 555 560

Glu Cys Gln Pro Ala Thr Glu Asn Gln Arg Val Pro Leu Ile Val Ala
 565 570 575

Ala Cys Cys Arg Ile Val Glu Ala Arg Gly Leu Glu Ser Thr Gly Ile
 580 585 590

Tyr Arg Val Pro Gly Asn Asn Ala Val Val Ser Ser Leu Gln Glu Gln
 595 600 605

674

Leu Asn Arg Gly Pro Gly Asp Ile Asn Leu Gln Asp Glu Arg Trp Gln
 610 615 620

Asp Leu Asn Val Ile Ser Ser Leu Leu Lys Ser Phe Phe Arg Lys Leu
 625 630 635 640

Pro Glu Pro Leu Phe Thr Asp Asp Lys Tyr Asn Asp Phe Ile Glu Ala
 645 650 655

Asn Arg Ile Glu Asp Ala Arg Glu Arg Met Arg Thr Leu Arg Lys Leu
 660 665 670

Ile Arg Asp Leu Pro Gly His Tyr Tyr Glu Thr Leu Lys Phe Leu Val
 675 680 685

Gly His Leu Lys Thr Ile Ala Asp His Ser Glu Lys Asn Lys Met Glu
 690 695 700

Pro Arg Asn Leu Ala Leu Val Phe Gly Pro Thr Leu Val Arg Thr Ser
 705 710 715 720

Glu Asp Asn Met Thr Asp Met Val Thr His Met Pro Asp Arg Tyr Lys
 725 730 735

Ile Val Glu Thr Leu Ile Gln His Ser Asp Trp Phe Phe Ser Asp Glu
 740 745 750

Glu Asp Lys Gly Glu Arg Thr Pro Val Gly Asp Lys Glu Pro Gln Ala
 755 760 765

Val Pro Asn Ile Glu Tyr Leu Leu Pro Asn Ile Gly Arg Thr Val Pro
 770 775 780

Pro Gly Asp Pro Gly Ser Asp Ser Thr Thr Cys Ser Ser Ala Lys Ser
 785 790 795 800

Lys Gly Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu Met Leu
 805 810 815

Ala Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys Arg Arg
 820 825 830

Glu Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu Gln Glu
 835 840 845

Ala His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln Glu Arg

675

850

855

860

Pro Pro Gly Ser Arg Gly Pro Ala Ala Ala Ala Asp Ala Pro Arg Arg
 865 870 875 880

Arg His Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala Gly Gly
 885 890 895

Ala Ala Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile Gln Pro
 900 905 910

Val Thr Met Asp Arg
 915

<210> 530
 <211> 851
 <212> PRT
 <213> Homo sapien

<400> 530

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

676

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser
 340 345 350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
 355 360 365

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
 370 375 380

677

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
 385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
 405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
 420 425 430

Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro
 435 440 445

Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys
 450 455 460

Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu
 465 470 475 480

Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile
 485 490 495

Arg Glu Asn Ser Arg Ala Glu Gly Glu Asp Pro Gly Cys Ala Asn Gln
 500 505 510

Ala Leu Ile Ser Lys Lys Leu Asn Asp Tyr Arg Lys Val Ser His Ser
 515 520 525

Ser Gly Pro Lys Ala Asp Ser Ser Pro Lys Gly Ser Arg Gly Leu Gly
 530 535 540

Gly Leu Lys Ser Glu Phe Leu Lys Gln Ser Ala Ala Arg Gly Leu Arg
 545 550 555 560

Thr Gln Asp Leu Pro Ala Gly Ser Lys Asp Asp Ser Ala Ala Ala Pro
 565 570 575

Lys Thr Pro Trp Gly Ile Asn Ile Ile Lys Lys Asn Lys Lys Ala Ala
 580 585 590

Pro Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu
 595 600 605

Asn Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu
 610 615 620

Ala Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn

678

| | | | | | | |
|---|-----|-----|--|-----|--|-----|
| 625 | | 630 | | 635 | | 640 |
| Ala Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp | | | | | | |
| | 645 | | | 650 | | 655 |
| Ile Asn Leu Gln Asp Glu Arg Trp Gln Asp Leu Asn Val Ile Ser Ser | | | | | | |
| | 660 | | | 665 | | 670 |
| Leu Leu Lys Ser Phe Phe Arg Lys Leu Pro Glu Pro Leu Phe Thr Asp | | | | | | |
| | 675 | | | 680 | | 685 |
| Asp Lys Tyr Asn Asp Phe Ile Glu Ala Asn Arg Ile Glu Asp Ala Arg | | | | | | |
| | 690 | | | 695 | | 700 |
| Glu Arg Met Arg Thr Leu Arg Lys Leu Ile Arg Asp Leu Pro Gly His | | | | | | |
| 705 | | 710 | | 715 | | 720 |
| Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala | | | | | | |
| | 725 | | | 730 | | 735 |
| Asp His Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val | | | | | | |
| | 740 | | | 745 | | 750 |
| Phe Gly Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met | | | | | | |
| | 755 | | | 760 | | 765 |
| Val Thr His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln | | | | | | |
| | 770 | | | 775 | | 780 |
| His Ser Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Thr | | | | | | |
| 785 | | 790 | | 795 | | 800 |
| Pro Val Gly Asp Lys Glu Pro Gln Ala Val Pro Asn Ile Glu Tyr Leu | | | | | | |
| | 805 | | | 810 | | 815 |
| Leu Pro Asn Ile Gly Arg Thr Val Pro Pro Gly Asp Pro Gly Ser Asp | | | | | | |
| | 820 | | | 825 | | 830 |
| Ser Thr Thr Cys Ser Ser Ala Lys Ser Lys Val Arg Met Lys Ala Ile | | | | | | |
| | 835 | | | 840 | | 845 |
| Leu Lys Ala | | | | | | |
| | 850 | | | | | |

<210> 531

<211> 926

679

<212> PRT

<213> Homo sapien

<400> 531

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15

Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30

Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45

Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60

Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80

Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95

Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110

Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125

Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140

Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160

Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175

Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190

Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205

Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220

680

Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240

Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His
 245 250 255

Val Pro Ala Ser Ala Val Val Ser Ser Ala Met Asn Ser Ala Pro Val
 260 265 270

Leu Gly Thr Ser Pro Ser Ser Pro Thr Phe Thr Phe Thr Leu Gly Arg
 275 280 285

His Tyr Ser Gln Asp Cys Ser Ser Ile Lys Ala Gly Arg Arg Ser Ser
 290 295 300

Tyr Leu Leu Ala Ile Thr Thr Glu Arg Ser Lys Ser Cys Asp Asp Gly
 305 310 315 320

Leu Asn Thr Phe Arg Asp Glu Gly Arg Val Leu Arg Arg Leu Pro Asn
 325 330 335

Arg Ile Pro Ser Leu Arg Met Leu Arg Ser Phe Phe Thr Asp Gly Ser
 340 345 350

Leu Asp Ser Trp Gly Thr Ser Glu Asp Ala Asp Ala Pro Ser Lys Arg
 355 360 365

His Ser Thr Ser Asp Leu Ser Asp Ala Thr Phe Ser Asp Ile Arg Arg
 370 375 380

Glu Gly Trp Leu Tyr Tyr Lys Gln Ile Leu Thr Lys Lys Gly Lys Lys
 385 390 395 400

Ala Gly Ser Gly Leu Arg Gln Trp Lys Arg Val Tyr Ala Ala Leu Arg
 405 410 415

Ala Arg Ser Leu Ser Leu Ser Lys Glu Arg Arg Glu Pro Gly Pro Ala
 420 425 430

Ala Ala Gly Ala Ala Ala Ala Gly Ala Gly Glu Asp Glu Ala Ala Pro
 435 440 445

Val Cys Ile Gly Ser Cys Leu Val Asp Ile Ser Tyr Ser Glu Thr Lys
 450 455 460

Arg Arg His Val Phe Arg Leu Thr Thr Ala Asp Phe Cys Glu Tyr Leu

681

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 465 | | 470 | | 475 | | 480 | | | | | | | | | |
| Phe | Gln | Ala | Glu | Asp | Arg | Asp | Asp | Met | Leu | Gly | Trp | Ile | Arg | Ala | Ile |
| | | | | 485 | | | | | 490 | | | | | 495 | |
| Arg | Glu | Asn | Ser | Arg | Ala | Glu | Gly | Glu | Asp | Pro | Gly | Cys | Ala | Asn | Gln |
| | | | 500 | | | | | 505 | | | | | 510 | | |
| Ala | Leu | Ile | Ser | Lys | Lys | Leu | Asn | Asp | Tyr | Arg | Lys | Val | Ser | His | Ser |
| | | 515 | | | | | 520 | | | | | 525 | | | |
| Ser | Gly | Pro | Lys | Ala | Asp | Ser | Ser | Pro | Lys | Gly | Ser | Arg | Gly | Leu | Gly |
| | 530 | | | | | 535 | | | | | 540 | | | | |
| Gly | Leu | Lys | Ser | Glu | Phe | Leu | Lys | Gln | Ser | Ala | Ala | Arg | Gly | Leu | Arg |
| 545 | | | | | 550 | | | | | 555 | | | | | 560 |
| Thr | Gln | Asp | Leu | Pro | Ala | Gly | Ser | Lys | Asp | Asp | Ser | Ala | Ala | Ala | Pro |
| | | | 565 | | | | | | 570 | | | | | 575 | |
| Lys | Thr | Pro | Trp | Gly | Ile | Asn | Ile | Ile | Lys | Lys | Asn | Lys | Lys | Ala | Ala |
| | | 580 | | | | | 585 | | | | | | | 590 | |
| Pro | Arg | Ala | Phe | Gly | Val | Arg | Leu | Glu | Glu | Cys | Gln | Pro | Ala | Thr | Glu |
| | | 595 | | | | | 600 | | | | | 605 | | | |
| Asn | Gln | Arg | Val | Pro | Leu | Ile | Val | Ala | Ala | Cys | Cys | Arg | Ile | Val | Glu |
| | 610 | | | | | 615 | | | | | 620 | | | | |
| Ala | Arg | Gly | Leu | Glu | Ser | Thr | Gly | Ile | Tyr | Arg | Val | Pro | Gly | Asn | Asn |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| Ala | Val | Val | Ser | Ser | Leu | Gln | Glu | Gln | Leu | Asn | Arg | Gly | Pro | Gly | Asp |
| | | | 645 | | | | | | 650 | | | | | 655 | |
| Ile | Asn | Leu | Gln | Asp | Glu | Arg | Trp | Gln | Asp | Leu | Asn | Val | Ile | Ser | Ser |
| | | 660 | | | | | | 665 | | | | | 670 | | |
| Leu | Leu | Lys | Ser | Phe | Phe | Arg | Lys | Leu | Pro | Glu | Pro | Leu | Phe | Thr | Asp |
| | | 675 | | | | | 680 | | | | | 685 | | | |
| Asp | Lys | Tyr | Asn | Asp | Phe | Ile | Glu | Ala | Asn | Arg | Ile | Glu | Asp | Ala | Arg |
| | 690 | | | | | 695 | | | | | 700 | | | | |
| Glu | Arg | Met | Arg | Thr | Leu | Arg | Lys | Leu | Ile | Arg | Asp | Leu | Pro | Gly | His |
| 705 | | | | | 710 | | | | | 715 | | | | | 720 |

682

Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly His Leu Lys Thr Ile Ala
 725 730 735

Asp His Ser Glu Lys Asn Lys Met Glu Pro Arg Asn Leu Ala Leu Val
 740 745 750

Phe Gly Pro Thr Leu Val Arg Thr Ser Glu Asp Asn Met Thr Asp Met
 755 760 765

Val Thr His Met Pro Asp Arg Tyr Lys Ile Val Glu Thr Leu Ile Gln
 770 775 780

His Ser Asp Trp Phe Phe Ser Asp Glu Glu Asp Lys Gly Glu Arg Ile
 785 790 795 800

Leu Pro Pro Val Val Gln Pro Ser Pro Arg Val Arg Gly Pro Pro Arg
 805 810 815

Arg Ser Arg Thr Pro Gly Arg Cys Trp Arg Ser Pro Ser Ser Arg Pro
 820 825 830

Ser Thr Ala Ser Ala Arg Ser Gly Gly Arg Arg Gly Gly Trp Ala Ala
 835 840 845

Ala Pro Thr Thr Thr Arg Ser Arg Arg Arg Thr Ser Leu Gly Arg Gly
 850 855 860

Pro Gln Arg Arg Gly Leu Arg Ser Gly Arg Arg Gly Ala Glu Ala Arg
 865 870 875 880

Arg Arg Arg Pro Leu Pro Arg Ala Ala Ala Thr Ala Ala Pro Gly Pro
 885 890 895

Gly Ser Pro Pro Ala Ala Arg Glu Gly Pro Pro Ala Ala Ala Thr Arg
 900 905 910

Ser Ile Val Ser Gly Tyr Ile Gln Pro Val Thr Met Asp Arg
 915 920 925

<210> 532

<211> 1011

<212> PRT

<213> Homo sapien

<400> 532

683

Met Ala Pro Arg Ala Arg Ser Ala Ser Gln Asp Arg Leu Glu Glu Val
 1 5 10 15
 Ala Ala Pro Arg Pro Trp Pro Cys Ser Thr Ser Gln Asp Ala Leu Ser
 20 25 30
 Gln Leu Gly Gln Glu Gly Trp His Arg Ala Arg Ser Asp Asp Tyr Leu
 35 40 45
 Ser Arg Ala Thr Arg Ser Ala Glu Ala Leu Gly Pro Gly Ala Leu Val
 50 55 60
 Ser Pro Arg Phe Glu Arg Cys Gly Trp Ala Ser Gln Arg Ser Ser Ala
 65 70 75 80
 Arg Thr Pro Ala Cys Pro Thr Arg Asp Leu Pro Gly Pro Gln Ala Pro
 85 90 95
 Thr Pro Ser Gly Leu Gln Gly Leu Asp Asp Leu Gly Tyr Ile Gly Tyr
 100 105 110
 Arg Ser Tyr Ser Pro Ser Phe Gln Arg Arg Thr Gly Leu Leu His Ala
 115 120 125
 Leu Ser Phe Arg Asp Ser Pro Phe Gly Gly Leu Pro Thr Phe Asn Leu
 130 135 140
 Ala Gln Ser Pro Ala Ser Phe Pro Pro Glu Ala Ser Glu Pro Pro Arg
 145 150 155 160
 Val Val Arg Pro Glu Pro Ser Thr Arg Ala Leu Glu Pro Pro Ala Glu
 165 170 175
 Asp Arg Gly Asp Glu Val Val Leu Arg Gln Lys Pro Pro Thr Gly Arg
 180 185 190
 Lys Val Gln Leu Thr Pro Ala Arg Gln Met Asn Leu Gly Phe Gly Asp
 195 200 205
 Glu Ser Pro Glu Pro Glu Ala Ser Gly Arg Gly Glu Arg Leu Gly Arg
 210 215 220
 Lys Val Ala Pro Leu Ala Thr Thr Glu Asp Ser Leu Ala Ser Ile Pro
 225 230 235 240
 Phe Ile Asp Glu Pro Thr Ser Pro Ser Ile Asp Leu Gln Ala Lys His

255

Phe Gln Ala Glu Asp Arg Asp Asp Met Leu Gly Trp Ile Arg Ala Ile
485 490 495

685

Arg Glu Asn Ser Arg Ala Glu Gly Glu Asp Pro Gly Cys Ala Asn Gln
 500 505 510

Ala Leu Ile Ser Lys Lys Leu Asn Asp Tyr Arg Lys Val Ser His Ser
 515 520 525

Ser Gly Pro Lys Ala Asp Ser Ser Pro Lys Gly Ser Arg Gly Leu Gly
 530 535 540

Gly Leu Lys Ser Glu Phe Leu Lys Gln Ser Ala Ala Arg Gly Leu Arg
 545 550 555 560

Thr Gln Asp Leu Pro Ala Gly Ser Lys Asp Asp Ser Ala Ala Ala Pro
 565 570 575

Lys Thr Pro Trp Gly Ile Asn Ile Ile Lys Lys Asn Lys Lys Ala Ala
 580 585 590

Pro Arg Ala Phe Gly Val Arg Leu Glu Glu Cys Gln Pro Ala Thr Glu
 595 600 605

Asn Gln Arg Val Pro Leu Ile Val Ala Ala Cys Cys Arg Ile Val Glu
 610 615 620

Ala Arg Gly Leu Glu Ser Thr Gly Ile Tyr Arg Val Pro Gly Asn Asn
 625 630 635 640

Ala Val Val Ser Ser Leu Gln Glu Gln Leu Asn Arg Gly Pro Gly Asp
 645 650 655

Ile Asn Leu Gln Asp Glu Arg Trp Gln Asp Leu Asn Val Ile Ser Ser
 660 665 670

Leu Leu Lys Ser Phe Phe Arg Lys Leu Pro Glu Pro Leu Phe Thr Asp
 675 680 685

Gly Ala Leu Leu Phe Tyr Leu Leu Asn Leu Gly Val His Val Leu Glu
 690 695 700

Thr Gly Ala Gly Thr Pro Phe Leu Gly Ser Ala Cys Ser Ser Asp Gly
 705 710 715 720

Ile Ala Ser Gln Met Asn Thr Ala Gly Leu Pro Gln Val Arg Cys Thr
 725 730 735

686

Pro Glu Cys Ser Cys Asp Lys Tyr Asn Asp Phe Ile Glu Ala Asn Arg
 740 745 750

Ile Glu Asp Ala Arg Glu Arg Met Arg Thr Leu Arg Lys Leu Ile Arg
 755 760 765

Asp Leu Pro Gly His Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly His
 770 775 780

Leu Lys Thr Ile Ala Asp His Ser Glu Lys Asn Lys Met Glu Pro Arg
 785 790 795 800

Asn Leu Ala Leu Val Phe Gly Pro Thr Leu Val Arg Thr Ser Glu Asp
 805 810 815

Asn Met Thr Asp Met Val Thr His Met Pro Asp Arg Tyr Lys Ile Val
 820 825 830

Glu Thr Leu Ile Gln His Ser Asp Trp Phe Phe Ser Asp Glu Glu Asp
 835 840 845

Lys Gly Glu Arg Thr Pro Val Gly Asp Lys Glu Pro Gln Ala Val Pro
 850 855 860

Asn Ile Glu Tyr Leu Leu Pro Asn Ile Gly Arg Thr Val Pro Pro Gly
 865 870 875 880

Asp Pro Gly Ser Asp Ser Thr Thr Cys Ser Ser Ala Lys Ser Lys Gly
 885 890 895

Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu Met Leu Ala Ile
 900 905 910

Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys Arg Arg Glu Ala
 915 920 925

Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu Gln Glu Ala His
 930 935 940

Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln Glu Arg Pro Pro
 945 950 955 960

Gly Ser Arg Gly Pro Ala Ala Ala Ala Asp Ala Pro Arg Arg Arg His
 965 970 975

687

Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala Gly Gly Ala Ala
 980 985 990

Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile Gln Pro Val Thr
 995 1000 1005

Met Asp Arg
 1010

<210> 533
 <211> 324
 <212> PRT
 <213> Homo sapien

<400> 533

Met Val Pro Phe Ser Ser Asp Leu Leu Asn Leu Gly Val His Val Leu
 1 5 10 15

Glu Thr Gly Ala Gly Thr Pro Phe Leu Gly Ser Ala Cys Ser Ser Asp
 20 25 30

Gly Ile Ala Ser Gln Met Asn Thr Ala Gly Leu Pro Gln Val Arg Cys
 35 40 45

Thr Pro Glu Cys Ser Cys Asp Lys Tyr Asn Asp Phe Ile Glu Ala Asn
 50 55 60

Arg Ile Glu Asp Ala Arg Glu Arg Met Arg Thr Leu Arg Lys Leu Ile
 65 70 75 80

Arg Asp Leu Pro Gly His Tyr Tyr Glu Thr Leu Lys Phe Leu Val Gly
 85 90 95

His Leu Lys Thr Ile Ala Asp His Ser Glu Lys Asn Lys Met Glu Pro
 100 105 110

Arg Asn Leu Ala Leu Val Phe Gly Pro Thr Leu Val Arg Thr Ser Glu
 115 120 125

Asp Asn Met Thr Asp Met Val Thr His Met Pro Asp Arg Tyr Lys Ile
 130 135 140

Val Glu Thr Leu Ile Gln His Ser Asp Trp Phe Phe Ser Asp Glu Glu
 145 150 155 160

Asp Lys Gly Glu Arg Thr Pro Val Gly Asp Lys Glu Pro Gln Ala Val
 165 170 175

688

Pro Asn Ile Glu Tyr Leu Leu Pro Asn Ile Gly Arg Thr Val Pro Pro
 180 185 190

Gly Asp Pro Gly Ser Asp Ser Thr Thr Cys Ser Ser Ala Lys Ser Lys
 195 200 205

Gly Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu Met Leu Ala
 210 215 220

Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys Arg Arg Glu
 225 230 235 240

Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu Gln Glu Ala
 245 250 255

His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln Glu Arg Pro
 260 265 270

Pro Gly Ser Arg Gly Pro Ala Ala Ala Asp Ala Pro Arg Arg Arg
 275 280 285

His Arg Gly Pro Arg Thr Arg Gln Ser Pro Gly Gly Ala Gly Gly Ala
 290 295 300

Ala Gly Arg Gly Asp Ala Leu His Cys Val Gly Leu Ile Gln Pro Val
 305 310 315 320

Thr Met Asp Arg

<210> 534

<211> 269

<212> PRT

<213> Homo sapien

<400> 534

Met Met Arg Pro Trp Val Thr Gly Leu Gly Leu Gly Leu Asp Glu Arg
 1 5 10 15

Leu Gly Ala Val Thr Trp Arg Gly Arg Thr Gly Asp Arg Arg Arg Gly
 20 25 30

Arg Gln Arg Gly Arg Val Arg Asp Ala Pro Arg Ile Leu Asp Leu Ser
 35 40 45

689

Pro Thr Gln Gly Ser Trp Ala Pro Lys Lys Glu Pro Tyr Ala Arg Glu
 50 55 60

Met Leu Ala Ile Ser Phe Ile Ser Ala Val Asn Arg Lys Arg Lys Lys
 65 70 75 80

Arg Arg Glu Ala Arg Gly Leu Gly Ser Ser Thr Asp Asp Asp Ser Glu
 85 90 95

Gln Glu Ala His Lys Pro Gly Ala Gly Ala Thr Ala Pro Gly Thr Gln
 100 105 110

Glu Arg Pro Leu Gly Pro Leu Pro Gly Ala Val Ala Pro Glu Ala Pro
 115 120 125

Gly Arg Leu Ser Pro Pro Ala Ala Pro Glu Glu Arg Pro Ala Ala Asp
 130 135 140

Thr Arg Ser Ile Val Ser Gly Tyr Ser Thr Leu Ser Thr Met Asp Arg
 145 150 155 160

Ser Val Cys Ser Gly Ala Ser Gly Arg Arg Ala Gly Ala Gly Asp Glu
 165 170 175

Ala Asp Asp Glu Arg Ser Glu Leu Ser His Val Glu Thr Asp Thr Glu
 180 185 190

Gly Ala Ala Gly Ala Gly Pro Gly Gly Arg Leu Thr Arg Arg Pro Ser
 195 200 205

Phe Ser Ser His His Leu Met Pro Cys Asp Thr Leu Ala Arg Arg Arg
 210 215 220

Leu Ala Arg Gly Arg Pro Asp Gly Glu Gly Ala Gly Arg Gly Gly Pro
 225 230 235 240

Arg Ala Pro Glu Pro Pro Gly Ser Ala Ser Ser Ser Ser Gln Glu Ser
 245 250 255

Leu Arg Pro Pro Ala Ala Ala Leu Ala Ser Arg Pro Ser
 260 265

<210> 535

<211> 325

<212> PRT

<213> Homo sapien

690

<220>
 <221> MISC_FEATURE
 <222> (42)..(42)
 <223> x= any amino acid

<220>
 <221> MISC_FEATURE
 <222> (44)..(44)
 <223> x= any amino acid

<220>
 <221> MISC_FEATURE
 <222> (64)..(64)
 <223> x= any amino acid

<400> 535

Met Glu Ser Trp Asn Trp Val Leu Val Phe Gly Cys Ile Leu Val Arg
 1 5 10 15

Met Ser Glu Asp Asn Met Ile Asp Met Val Thr Tyr Met Leu Asp Cys
 20 25 30

Tyr Lys Ile Val Glu Thr Leu Ile Gln Xaa Leu Xaa Trp Phe Phe Ser
 35 40 45

Asp Glu Glu Asp Lys Gly Glu Arg Thr Leu Val Gly Asp Lys Glu Xaa
 50 55 60

Gln Ala Val Pro Asn Ile Glu Tyr Leu Leu Pro Asn Ile Trp Gln Asp
 65 70 75 80

Ser Ala Pro Trp Arg Pro Gly Val Ser Gly Pro Val Gly Asp Leu Lys
 85 90 95

Asp Ser Thr Thr Cys Ser Ser Ala Lys Ser Lys Gly Ser Trp Ala Pro
 100 105 110

Lys Lys Glu Pro Tyr Ala Arg Glu Met Leu Ala Ile Ser Phe Ile Ser
 115 120 125

Ala Val Asn Arg Lys Arg Lys Lys Arg Arg Glu Ala Arg Gly Leu Gly
 130 135 140

Ser Ser Thr Asp Asp Asp Ser Glu Gln Glu Ala His Lys Pro Gly Ala
 145 150 155 160

Gly Ala Thr Ala Pro Gly Thr Gln Glu Arg Pro Leu Gly Pro Leu Pro

691

165

170

175

Gly Ala Val Ala Pro Glu Ala Pro Gly Arg Leu Ser Pro Pro Ala Ala
 180 185 190

Pro Glu Glu Arg Pro Ala Ala Asp Thr Arg Ser Ile Val Ser Gly Tyr
 195 200 205

Ser Thr Leu Ser Thr Met Asp Arg Ser Val Cys Ser Gly Ala Ser Gly
 210 215 220

Arg Arg Ala Gly Ala Gly Asp Glu Ala Asp Asp Glu Arg Ser Glu Leu
 225 230 235 240

Ser His Val Glu Thr Asp Thr Glu Gly Ala Ala Gly Ala Gly Pro Gly
 245 250 255

Gly Arg Leu Thr Arg Arg Pro Ser Phe Ser Ser His His Leu Met Pro
 260 265 270

Cys Asp Thr Leu Ala Arg Arg Arg Leu Ala Arg Gly Arg Pro Asp Gly
 275 280 285

Glu Gly Ala Gly Arg Gly Gly Pro Arg Ala Pro Glu Pro Pro Gly Ser
 290 295 300

Ala Ser Ser Ser Ser Gln Glu Ser Leu Arg Pro Pro Ala Ala Ala Leu
 305 310 315 320

Ala Ser Arg Pro Ser
 325

<210> 536

<211> 51

<212> PRT

<213> Homo sapien

<400> 536

Met Glu Leu Ser Ile Val Pro Val Thr Tyr Lys Thr Met Ser Pro Leu
 1 5 10 15

His Ile His Phe Tyr Leu Leu Leu Trp Lys Ser Ala Val Asn Asn Asp
 20 25 30

Ile Cys Thr Val Glu Ile Phe Phe Lys Val Leu Ala Pro Pro Pro Thr
 35 40 45

692

Leu Val Val
50

<210> 537
<211> 41
<212> PRT
<213> Homo sapien

<400> 537

Met Asn Lys Thr Lys Phe Ser Leu Pro Asn Asp Phe Leu Ser His Leu
1 5 10 15

Gly Asp Val Thr Leu Ala Ser Ser Leu Thr Pro Leu Ser Phe Ile Ile
20 25 30

His Thr Asn Ser Leu Ala Gly Phe Thr
35 40

<210> 538
<211> 108
<212> PRT
<213> Homo sapien

<400> 538

Met Ala Lys Leu Asp Lys Asn Pro Gly Leu Leu Thr Pro Thr Arg Glu
1 5 10 15

Pro Thr Pro Ser Thr Phe Ala Gly Arg His Val Met Asp Thr Thr Pro
20 25 30

Glu Lys Gln Glu Pro Gly Val Arg Leu Glu Thr Cys Leu Arg Leu Ala
35 40 45

Met Arg Asn Ala Pro Gly Arg His Glu Trp Pro Tyr Thr Phe Pro Pro
50 55 60

Ser Pro Ala Pro Ser Phe Lys Val Pro Ile His Val Leu Ala Pro Ile
65 70 75 80

Pro Leu Gly Ser Phe Gly Ala Ser His Leu His Thr Arg Thr His Thr
85 90 95

Val Asn Trp Ala Leu Leu Ser Pro Cys Pro Val His
100 105

<210> 539
<211> 119

693

<212> PRT

<213> Homo sapien

<400> 539

Arg Ala Phe Leu Asp Phe Val Cys Arg Thr Pro Ala Val Pro Phe Pro
 1 5 10 15

Arg His Ser Pro Pro Glu His Thr Gly Arg Gly Gly Ser Pro Lys Thr
 20 25 30

Trp Pro Pro Leu Ile Pro Val Leu Cys Val Ser Pro Phe Glu Phe Leu
 35 40 45

Thr Ser Ser Ser Trp Val Leu Phe Leu Leu Ser Pro Phe Leu Phe Leu
 50 55 60

Arg Lys Pro Gln Ala Ala Ser Pro Arg Ala Leu Val Trp Pro Glu Thr
 65 70 75 80

Glu Ala Pro Arg Leu Glu Gly Gly Ala Ala Leu Gly Gly Pro Gly Gln
 85 90 95

Trp Lys Ala Cys Tyr Tyr Leu Glu Trp Leu Leu Gly Pro Asn Thr Ser
 100 105 110

Trp Glu Ala Gly Trp Val Lys
 115

<210> 540

<211> 537

<212> PRT

<213> Homo sapien

<400> 540

Met Glu Ser Gly Leu Ala Gly Asn Gly Thr Gly Ala Gly Leu Val Met
 1 5 10 15

Lys Val Lys Gln Glu Lys Pro Glu Arg Leu Leu Gln Thr Leu Ala Pro
 20 25 30

Gln Ala Met Leu Val Glu Lys Asp Lys Glu Asn Ile Phe Gln Gln His
 35 40 45

Arg Gly Leu Pro Pro Arg Gln Thr Met Gly Arg Pro Arg Ala Leu Gly
 50 55 60

Gly Gln Glu Glu Ser Gly Ser Pro Arg Trp Ala Pro Pro Thr Glu Gln

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| 65 | | | | 70 | | | | 75 | | | | 80 | | | | |
| Asp | Ala | Gly | Leu | Ala | Gly | Arg | Ala | Pro | Gly | Ser | Ala | Ser | Gly | Pro | Leu | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| Ser | Pro | Ser | Leu | Ser | Ser | Gly | Glu | Gly | His | Phe | Val | Cys | Leu | Asp | Cys | |
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| Gly | Lys | Arg | Phe | Ser | Trp | Trp | Ser | Ser | Leu | Lys | Ile | His | Gln | Arg | Thr | |
| | | | | 115 | | | | | 120 | | | | | 125 | | |
| His | Thr | Gly | Glu | Lys | Pro | Tyr | Leu | Cys | Gly | Lys | Cys | Gly | Lys | Ser | Phe | |
| | | | | 130 | | | | | 135 | | | | | 140 | | |
| Ser | Gln | Lys | Pro | Asn | Leu | Ala | Arg | His | Gln | Arg | His | His | Thr | Gly | Glu | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| Arg | Pro | Phe | Cys | Cys | Pro | Glu | Cys | Ala | Arg | Arg | Phe | Ser | Gln | Lys | Gln | |
| | | | | 165 | | | | | 170 | | | | | 175 | | |
| His | Leu | Leu | Lys | His | Gln | Lys | Thr | His | Ser | Arg | Pro | Ala | Thr | His | Ser | |
| | | | | 180 | | | | | 185 | | | | | 190 | | |
| Cys | Pro | Glu | Cys | Glu | Arg | Cys | Phe | Arg | His | Gln | Val | Gly | Leu | Arg | Ile | |
| | | | | 195 | | | | | 200 | | | | | 205 | | |
| His | Gln | Arg | Ala | His | Ala | Arg | Asp | Arg | Gln | Gly | Ser | Arg | Ala | Gly | Leu | |
| | | | | 210 | | | | | 215 | | | | | 220 | | |
| His | Glu | Leu | Ile | Gln | Asp | Ala | Ala | Ala | Arg | Arg | Ala | Cys | Arg | Leu | Gln | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| Pro | Gly | Pro | Pro | Arg | Gly | Arg | Pro | Glu | Trp | Ala | Trp | Leu | Gly | Leu | Cys | |
| | | | | 245 | | | | | 250 | | | | | 255 | | |
| Gln | Gly | Trp | Trp | Gly | Gln | Pro | Gly | Ala | Arg | Ala | Ala | Val | Ser | Gly | Pro | |
| | | | | 260 | | | | | 265 | | | | | 270 | | |
| Glu | Gly | Pro | Gly | Glu | Pro | Arg | Gln | Phe | Ile | Cys | Asn | Glu | Cys | Gly | Lys | |
| | | | | 275 | | | | | 280 | | | | | 285 | | |
| Ser | Phe | Thr | Trp | Trp | Ser | Ser | Leu | Asn | Ile | His | Gln | Arg | Ile | His | Thr | |
| | | | | 290 | | | | | 295 | | | | | 300 | | |
| Gly | Glu | Arg | Pro | Tyr | Ala | Cys | Pro | Glu | Cys | Gly | Arg | Arg | Phe | Ser | Gln | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | |

695

Lys Pro Asn Leu Thr Arg His Leu Arg Asn His Thr Gly Glu Arg Pro
 325 330 335

His Pro Cys Pro His Cys Gly Arg Gly Phe Arg Gln Lys Gln His Leu
 340 345 350

Leu Lys His Leu Arg Thr His Leu Pro Gly Ala Gln Ala Ala Pro Cys
 355 360 365

Pro Ser Cys Gly Lys Ser Cys Arg Ser Arg Ala Ala Leu Arg Ala His
 370 375 380

Gln Arg Ala His Ala Val Ala Glu Pro Ala Val Pro Ala Gly Glu Pro
 385 390 395 400

Gly Asp Gln Pro Gln Ala Glu Ala Ile Pro Gly Leu Ala Ala Arg Pro
 405 410 415

Arg Ser Ser Gln Arg Ser Pro Gly Ala Arg Asp Thr Leu Trp Gly Arg
 420 425 430

Gly Gln Ala Gly Leu Ala Gly Pro Gly Glu Pro Arg Gln Phe Ile Cys
 435 440 445

Asn Glu Cys Gly Lys Ser Phe Ser Trp Trp Ser Ala Leu Thr Ile His
 450 455 460

Gln Arg Ile His Thr Gly Glu Arg Pro Tyr Pro Cys Pro Glu Cys Gly
 465 470 475 480

Arg Arg Phe Ser Gln Lys Pro Asn Leu Thr Arg His Arg Arg Asn His
 485 490 495

Thr Gly Glu Arg Pro Tyr Leu Cys Pro Ala Cys Gly Arg Gly Phe Ser
 500 505 510

Gln Lys Gln His Leu Leu Lys His Gln Arg Val His Arg Ala Ala Pro
 515 520 525

Ala Cys Ser Pro Lys Glu Glu Ala Arg
 530 535

<210> 541

<211> 68

<212> PRT

696

<213> Homo sapien

<400> 541

Met Glu Ser Gly Leu Ala Gly Asn Gly Thr Gly Ala Gly Leu Val Met
 1 5 10 15

Lys Val Lys Gln Glu Lys Pro Glu Arg Leu Leu Gln Thr Leu Ala Pro
 20 25 30

Gln Ala Met Leu Val Glu Lys Asp Lys Glu Asn Val Leu Trp Thr Thr
 35 40 45

Leu Val Phe Phe Phe Ala Cys Gly Ser Phe Lys Leu Leu Val Phe Lys
 50 55 60

Ile Ser Thr Phe
 65

<210> 542

<211> 550

<212> PRT

<213> Homo sapien

<400> 542

Met Leu Asp Leu Met Leu Glu Ala Val Asn Asn Ile Lys Asp Ala Met
 1 5 10 15

Pro Lys Met Gln Ile Gly Ala Pro Val Gln Ala Ile Thr Leu Met Ser
 20 25 30

Gly Glu Arg Pro Cys Leu Gln Gly Tyr Tyr Thr Ala Ala Val Ile Asp
 35 40 45

Ser Leu Ser Leu Thr Val His Leu Arg Ile Leu Asn Ala Pro Gly Ala
 50 55 60

Ser Gly Asn Ser Ile Gln Asp Tyr Thr Asn Leu Ser Val Val Arg Ala
 65 70 75 80

Lys Gly Asn Lys Asp Val Gly Lys Ser Lys His Cys Phe Asn Ala Phe
 85 90 95

Ala Ser Asp Arg Ser Ser Leu His Arg Asp Leu Gly Pro Asp Thr Arg
 100 105 110

Pro Pro Glu Cys Ile Val Leu Tyr Asn Phe Lys Arg Cys Gly Lys Arg
 115 120 125

Phe Ser Trp Trp Ser Ser Leu Lys Ile His Gln Arg Thr His Thr Gly
 130 135 140

Glu Lys Pro Tyr Leu Cys Gly Lys Cys Gly Lys Ser Phe Ser Gln Lys
 145 150 155 160

Pro Asn Leu Ala Arg His Gln Arg His His Thr Gly Glu Arg Pro Phe
 165 170 175

Cys Cys Pro Glu Cys Ala Arg Arg Phe Ser Gln Lys Gln His Leu Leu
 180 185 190

Lys His Gln Lys Thr His Ser Arg Pro Ala Thr His Ser Cys Pro Glu
 195 200 205

Cys Glu Arg Cys Phe Arg His Gln Val Gly Leu Arg Ile His Gln Arg
 210 215 220

Ala His Ala Arg Asp Arg Gln Gly Ser Arg Ala Gly Leu His Glu Leu
 225 230 235 240

Ile Gln Asp Ala Ala Ala Arg Arg Ala Cys Arg Leu Gln Pro Gly Pro
 245 250 255

Pro Arg Gly Arg Pro Glu Trp Ala Trp Leu Gly Leu Cys Gln Gly Trp
 260 265 270

Trp Gly Gln Pro Gly Ala Arg Ala Ala Val Ser Gly Pro Glu Gly Pro
 275 280 285

Gly Glu Pro Arg Gln Phe Ile Cys Asn Glu Cys Gly Lys Ser Phe Thr
 290 295 300

Trp Trp Ser Ser Leu Asn Ile His Gln Arg Ile His Thr Gly Glu Arg
 305 310 315 320

Pro Tyr Ala Cys Pro Glu Cys Gly Arg Arg Phe Ser Gln Lys Pro Asn
 325 330 335

Leu Thr Arg His Leu Arg Asn His Thr Gly Glu Arg Pro His Pro Cys
 340 345 350

Pro His Cys Gly Arg Gly Phe Arg Gln Lys Gln His Leu Leu Lys His
 355 360 365

698

Leu Arg Thr His Leu Pro Gly Ala Gln Ala Ala Pro Cys Pro Ser Cys
 370 375 380

Gly Lys Ser Cys Arg Ser Arg Ala Ala Leu Arg Ala His Gln Arg Ala
 385 390 395 400

His Ala Val Ala Glu Pro Ala Val Pro Ala Gly Glu Pro Gly Asp Gln
 405 410 415

Pro Gln Ala Glu Ala Ile Pro Gly Leu Ala Ala Arg Pro Arg Ser Ser
 420 425 430

Gln Arg Ser Pro Gly Ala Arg Asp Thr Leu Trp Gly Arg Gly Gln Ala
 435 440 445

Gly Leu Ala Gly Pro Gly Glu Pro Arg Gln Phe Ile Cys Asn Glu Cys
 450 455 460

Gly Lys Ser Phe Ser Trp Trp Ser Ala Leu Thr Ile His Gln Arg Ile
 465 470 475 480

His Thr Gly Glu Arg Pro Tyr Pro Cys Pro Glu Cys Gly Arg Arg Phe
 485 490 495

Ser Gln Lys Pro Asn Leu Thr Arg His Arg Arg Asn His Thr Gly Glu
 500 505 510

Arg Pro Tyr Leu Cys Pro Ala Cys Gly Arg Gly Phe Ser Gln Lys Gln
 515 520 525

His Leu Leu Lys His Gln Arg Val His Arg Ala Ala Pro Ala Cys Ser
 530 535 540

Pro Lys Glu Glu Ala Arg
 545 550

<210> 543
 <211> 198
 <212> PRT
 <213> Homo sapien

<400> 543

Met Glu Ser Gly Leu Ala Gly Asn Gly Thr Gly Ala Gly Leu Val Met
 1 5 10 15

Lys Val Lys Gln Glu Lys Pro Glu Arg Leu Leu Gln Thr Leu Ala Pro

699

| | | |
|---|-----|-----|
| 20 | 25 | 30 |
| Gln Ala Met Leu Val Glu Lys Asp Lys Glu Asn Ile Phe Gln Gln His | | |
| 35 | 40 | 45 |
| Arg Gly Leu Pro Pro Arg Gln Thr Met Gly Arg Pro Arg Ala Leu Gly | | |
| 50 | 55 | 60 |
| Gly Gln Glu Glu Ser Gly Ser Pro Arg Trp Ala Pro Pro Thr Glu Gln | | |
| 65 | 70 | 75 |
| 80 | | |
| Asp Ala Gly Leu Ala Gly Arg Ala Pro Gly Ser Ala Ser Gly Pro Leu | | |
| 85 | 90 | 95 |
| Ser Pro Ser Leu Ser Ser Gly Glu Gly His Phe Val Cys Leu Asp Cys | | |
| 100 | 105 | 110 |
| Gly Lys Arg Phe Ser Trp Trp Ser Ser Leu Lys Ile His Gln Arg Thr | | |
| 115 | 120 | 125 |
| His Thr Gly Glu Lys Pro Tyr Leu Cys Gly Lys Cys Gly Lys Ser Phe | | |
| 130 | 135 | 140 |
| Ser Gln Lys Pro Asn Leu Ala Arg His Gln Arg His His Thr Gly Glu | | |
| 145 | 150 | 155 |
| 160 | | |
| Arg Pro Phe Cys Cys Pro Glu Cys Ala Arg Arg Phe Ser Gln Lys Gln | | |
| 165 | 170 | 175 |
| His Leu Leu Lys His Gln Arg Val His Arg Ala Ala Pro Ala Cys Ser | | |
| 180 | 185 | 190 |
| Pro Lys Glu Glu Ala Arg | | |
| 195 | | |
| <210> 544 | | |
| <211> 20 | | |
| <212> PRT | | |
| <213> Homo sapien | | |
| <400> 544 | | |
| Met Lys Leu Ile Ser Phe Ser Leu Met Leu Trp Leu Arg Val Asn Ala | | |
| 1 | 5 | 10 |
| 15 | | |
| Leu Tyr Leu Cys | | |
| 20 | | |

700

<210> 545
<211> 52
<212> PRT
<213> Homo sapien

<400> 545

Met His Cys Arg Gln Trp Glu Asn Lys Tyr Ser Met Asn Val Ser Glu
1 5 10 15

Lys Arg Lys Lys Arg Gly Leu Phe Val Tyr Tyr Ser Phe Lys Trp Lys
20 25 30

Asp Gln Gly His Gly Met Asn Tyr Ile Phe His Ile Leu Cys Ile Ser
35 40 45

Tyr Leu Phe Leu
50

<210> 546
<211> 67
<212> PRT
<213> Homo sapien

<400> 546

Met Leu Ile Lys Gln Ala Gly Val Arg Met Glu Asn Ala Ser Ile Arg
1 5 10 15

Lys Arg Thr His Lys Cys Leu Ala Ser Leu His Arg Val Phe Pro Leu
20 25 30

Leu Ser Ser Trp Ser Ser Pro Leu Gly Arg Asn Ser Pro Leu Gly His
35 40 45

Val Trp Ala Leu Ala Ser Ser Lys Leu Leu Tyr Pro Ser Ser Gly Glu
50 55 60

Asn Ser Leu
65

<210> 547
<211> 118
<212> PRT
<213> Homo sapien

<400> 547

Met Ala Glu Gln Ala Ser His Tyr Tyr Ala Arg Leu Gly Gly Ala
1 5 10 15

701

Arg Gln Lys Ile Ala Leu Gly Asp Thr Cys Leu Val Cys Arg Asp Pro
 20 25 30

Gln Gly Thr Ser Arg Val Leu Glu His Leu Leu Val Ser Phe Phe Leu
 35 40 45

Glu Leu Ser Tyr Phe Tyr Pro Lys Thr Asp Arg Ser Tyr Val Asn Leu
 50 55 60

His Leu Lys Lys Asp Ile Ala Phe Phe Pro Ser Ala Ser Gln Ile Cys
 65 70 75 80

Ser Asn Thr Asn Ser Leu Ala Phe Asp Phe Ile Ile Met Ile Val His
 85 90 95

Gln Pro Phe Phe Thr Lys Asn Pro His Ile Met Ser Tyr Lys Gly Phe
 100 105 110

Ile Ile Phe Asn Gly Lys
 115

<210> 548

<211> 115

<212> PRT

<213> Homo sapien

<400> 548

Met Gly Thr Glu Tyr Ser Ile Ala Leu Gln Met Ser Asn Ile Phe Lys
 1 5 10 15

Ala Met Leu Ser Asn Asn Val Tyr Thr Glu Asn Arg Met His Arg Phe
 20 25 30

Asn Ile Asp Ser Asn Val Tyr Val Gly Ser Phe Val Gly Asp Cys Lys
 35 40 45

Leu Tyr Val Pro Pro Val Leu Leu Gly Phe Val Gly Lys Leu Lys Glu
 50 55 60

Asn Leu Val Leu Ser Leu Ile Met Lys Phe Ile Ala Asn Leu Glu Arg
 65 70 75 80

Glu Asn Asn Leu Lys Thr Lys Ile Pro His Ser Ser Glu Asp Ala Trp
 85 90 95

Asn Lys Ile Trp Asn Ser Ser Val Pro Thr Ser Pro Leu Gln Thr Phe

702

100

105

110

Leu Leu Phe
115

<210> 549
<211> 63
<212> PRT
<213> Homo sapien

<400> 549

Met Lys Glu Ser Ile Val Arg His Tyr Ser Lys Lys Asn Phe Leu Thr
1 5 10 15

Cys Leu Ser Trp Lys Ser Thr Lys Gly His Leu Ser Cys Leu Asp Met
20 25 30

Asp Tyr Gln Tyr Val Cys Ile Gln His Thr Ala Tyr Lys Val Arg Gly
35 40 45

Asn Asn Arg Gln Tyr Ile Leu Cys Thr His Asn Tyr Ser Pro Pro
50 55 60

<210> 550
<211> 57
<212> PRT
<213> Homo sapien

<400> 550

Met Leu Phe Gly Thr Ile Lys Tyr Gln Ile Ile Ser Lys Lys Pro Met
1 5 10 15

Val Ser Trp Leu Cys Trp Cys Pro Ser Leu Thr Phe Val Ser Ser Trp
20 25 30

Gly Ser Arg Leu Ala Gly Cys Ser Ser Ser Leu Gln Asp Gly Ser Cys
35 40 45

Gly Pro Leu Ser His His Thr Gly Leu
50 55

<210> 551
<211> 41
<212> PRT
<213> Homo sapien

<400> 551

Met Ser Thr Phe Ser Ser Asp Leu Thr Ser Val Ser Thr Cys Leu Leu

703

1 5 10 15

Asp Ile Tyr Ile Tyr Leu Asp Met Ser Cys Gly Tyr Val Pro Arg Gln
 20 25 30

His Ile Gln Lys Leu Thr His Tyr Leu
 35 40

<210> 552
 <211> 92
 <212> PRT
 <213> Homo sapien

<400> 552

Met Leu Tyr Ser Phe Leu Asn Tyr Leu Asp Ile Ser Ser Ile Lys Leu
 1 5 10 15

Trp Pro Cys Val Pro Leu Gln Gly Ser Ser Ser Glu Met Thr Leu Ile
 20 25 30

Ser Cys Cys Ser Met Tyr Gln Ile His Ser Leu Val Tyr Cys Leu Asp
 35 40 45

Val Ser Thr Leu Cys Leu Gly Met Ile Cys Leu Thr Glu Met Asn Tyr
 50 55 60

Ile Tyr Val Pro Lys Ser Leu Ser Asn Phe Asn Ser Lys Tyr Ile Thr
 65 70 75 80

Ser Ser Ser Ile Gly Tyr Leu Phe His Ser Ala Phe
 85 90

<210> 553
 <211> 67
 <212> PRT
 <213> Homo sapien

<400> 553

Met Ile Phe Lys Arg Thr Phe Lys Ile Ser Thr His Leu Thr Thr Ile
 1 5 10 15

Leu Ser Arg Leu Cys Thr His Val Leu Gly Lys Leu Gln Lys Asn Gly
 20 25 30

Arg Lys Lys Gly Pro Lys Ser Thr Lys His Arg Arg His Asn Ser Lys
 35 40 45

704

Asn Ile Gln Tyr Tyr Cys Ser Lys Leu Leu Asn Lys Cys Ser Leu Thr
 50 55 60

Glu Asn His
 65

<210> 554
 <211> 57
 <212> PRT
 <213> Homo sapien
 <400> 554

Met Ala Asp Thr Val Ser Phe Ala Pro Ser Thr Ser Pro Ile Ser Leu
 1 5 10 15

Phe Phe Tyr Glu Cys Leu Pro Ser Pro Thr Pro Tyr Ala Pro Val Gly
 20 25 30

Phe His His Phe Ala Leu Phe Val Gln Lys Gly Val Pro Gly Leu Val
 35 40 45

Lys Gln Gly Pro Pro Ser Phe Cys Leu
 50 55

<210> 555
 <211> 73
 <212> PRT
 <213> Homo sapien
 <400> 555

Met Ser Val Gly Leu Met Asn His Leu Lys Leu Phe Lys Ser Arg Ala
 1 5 10 15

Glu Ala Ser Leu Lys Lys Glu Ile Ala Pro Phe Ser Ser Ile Phe Leu
 20 25 30

Ser Trp Val Ser Val Pro Ser Glu Pro Ser Trp Gly Ile Ala Ile Cys
 35 40 45

Phe Leu Gln Leu Leu Ser Gln Ser His Ser Gly Ile Arg Lys Phe Leu
 50 55 60

Ala Ile Asn His Leu Tyr Met Ser Tyr
 65 70

<210> 556
 <211> 43
 <212> PRT

705

<213> Homo sapien

<400> 556

Met Ser Phe Pro Leu Ile Met Lys His Ser Leu Lys Leu Phe Trp Tyr
 1 5 10 15

Val Ile Ile Leu Leu Tyr Ser Leu Tyr Thr Val Glu Asn Lys Phe Ser
 20 25 30

Ser Gly Ile Leu Val Ser Ser Ser Phe Ser Pro
 35 40

<210> 557

<211> 77

<212> PRT

<213> Homo sapien

<400> 557

Met Ala Ser Gln Tyr Leu Leu Cys Ile Phe Lys Gln Ile Lys Asn Val
 1 5 10 15

Ile Leu Thr Phe Ala Tyr Gly His Ser Tyr Asp Tyr Thr Glu Arg Asp
 20 25 30

Gly Ile Ile Leu Thr Cys Leu Ile His Gly Leu Phe Leu Val Asn Asn
 35 40 45

Asn Ile Thr Thr Gln Arg Lys Gly Asn Val Tyr Ile Leu Lys Asn Tyr
 50 55 60

Cys Gln Leu His Leu Val Phe Phe Arg Leu Cys Ile Lys
 65 70 75

<210> 558

<211> 61

<212> PRT

<213> Homo sapien

<400> 558

Met Ala Gly Ser Trp Val Ala Glu Ser Pro Pro Leu Gly Ala Gly Arg
 1 5 10 15

Ser Glu Cys Gln Pro Ser Ala Leu Ile Asn Leu Pro Asn His Leu Ile
 20 25 30

Ser Leu Ser Leu Ile Val Pro Ile Cys Phe Asn Gly Glu Gln Pro His
 35 40 45

706

Val Ile Leu Pro Asn Leu Ala Glu Ser Leu Arg Ile Ser
50 55 60

<210> 559
<211> 59
<212> PRT
<213> Homo sapien

<400> 559

Ala Ala Ala Gly Ser Gly Val Arg Ser Arg Asp Ala Val Val Gly Ala
1 5 10 15

Gly Gln Arg Arg Ala Pro Glu Ala Gly Ala Ala Gly Gly Arg Ala Asn
20 25 30

Val Ile Phe Pro Asn Lys Leu Phe Pro Ala Glu Ser Ser Leu Leu Ala
35 40 45

Gln Asn Lys Gln Met Lys Ser Ser Pro Glu Arg
50 55

<210> 560
<211> 55
<212> PRT
<213> Homo sapien

<400> 560

Ala Ala Ala Gly Ser Gly Val Arg Ser Arg Asp Ala Val Val Gly Ala
1 5 10 15

Gly Gln Arg Arg Ala Pro Glu Ala Gly Ala Ala Gly Gly Arg Ala Asn
20 25 30

Val Ile Phe Pro Asn Lys Leu Phe Pro Ala Glu Ser Ser Leu Leu Ala
35 40 45

Gln Asn Lys Gln Met Lys Arg
50 55

<210> 561
<211> 72
<212> PRT
<213> Homo sapien

<400> 561

Met Pro Cys Thr Val Ser Pro Ser Gln Gln Pro Arg Leu Gln Met Asp
1 5 10 15

707

Leu Pro Cys Ser Phe Pro Cys Pro Leu Asp Ser Trp Ser Ala Gly Leu
 20 25 30

Val Val Cys Pro Ala Leu Cys Gln Ala Ala Trp Arg Arg Gly His Leu
 35 40 45

Ala Ala Pro Leu Gly Phe Phe His Ala Thr Leu Val His Leu Ser Phe
 50 55 60

Leu Ser Gly Ala Gly Pro Arg Ile
 65 70

<210> 562
 <211> 121
 <212> PRT
 <213> Homo sapien

<400> 562

Met Thr Pro Pro Ala Phe Pro Leu Thr Ile Phe Ser Arg Asp Pro Pro
 1 5 10 15

Leu Leu Leu Gly Pro Lys Glu Glu Arg Gly Arg Lys Phe His Thr Pro
 20 25 30

Ser Lys Ala Arg Gly His Arg Arg Gly Gly Ser Arg Gln Ala Gly Ala
 35 40 45

Arg Cys Pro Ser Leu Gly Ala Ser Glu Gly His Thr Val Ala Arg Gln
 50 55 60

Pro Leu Leu Pro Leu Leu Pro Thr Trp Arg Pro Val Ala Lys Ala Phe
 65 70 75 80

Val Pro Gly Ser Glu Glu Leu Ala Val Leu Ala Ala Thr Pro Val His
 85 90 95

Gly Phe Pro Leu Ala Ser Ser Pro Arg Glu Phe Trp Leu Arg Glu Gly
 100 105 110

Val Arg Glu Glu Arg Lys Gly Thr Leu
 115 120

<210> 563
 <211> 57
 <212> PRT
 <213> Homo sapien

708

<400> 563

Met Gln Leu Lys Val Ser Gln Phe Ile Pro Arg Ile Ser His His Leu
 1 5 10 15

Gln Ala Pro Tyr Leu Asp Gly Ser Leu Ala Cys His Phe Phe Phe Phe
 20 25 30

Ser Pro Asn Val Thr Phe Ser Val Arg Ile Ser Leu Thr Ser Pro Phe
 35 40 45

Lys Ile Ala Thr Ser Thr Ser Thr Leu
 50 55

<210> 564

<211> 321

<212> PRT

<213> Homo sapien

<400> 564

Phe Val Ser Leu Cys Ser Gly Ser Ser Ser Cys Arg Ser Leu Leu Phe
 1 5 10 15

Phe Phe Arg Phe Val Leu Ile Arg Trp Ser Phe Pro Leu Leu Ser Ser
 20 25 30

Ser Phe Ser Ser Ser Leu Phe Val Val Leu Phe Arg Arg Cys Gly Leu
 35 40 45

Val Arg Phe Ser Arg Ser Val Leu Ala Ser Val Leu Leu Ala Leu Leu
 50 55 60

Leu Leu Ser Ser Cys Val Arg Phe Pro Val Ala Cys Leu Ser Phe Ser
 65 70 75 80

Leu Leu Leu Val Ile Cys Phe Ser Leu Phe Leu Leu Phe Leu Ser Pro
 85 90 95

Val Ser Pro Ser Phe Leu Val Ser Ser Ser Pro Phe Leu Leu Phe Ala
 100 105 110

Cys Ala Cys Leu Ala Arg Ser Val Phe Phe Cys Leu Cys Phe Cys Arg
 115 120 125

Val Arg Leu Ser Leu Val Phe Phe Gly Leu Leu Phe Leu Phe Ser Pro
 130 135 140

709

Leu Arg Ser Leu Leu Phe Ser Val Leu Arg Ala Ser Val Pro Phe Val
 145 150 155 160

Phe Phe Val Phe Phe Ala Ser Phe Arg Ser Leu Arg Ser Ser Ser Ser
 165 170 175

Val Pro Leu Leu Ser Ser Phe Leu Pro Leu Ser Pro Phe Leu Leu Leu
 180 185 190

Trp Leu Pro Ser Leu Ala Val Leu Pro Leu Arg Leu Pro Leu Leu Pro
 195 200 205

Ser Val Val Ser Arg Cys Cys Ser Cys Val Leu Leu Cys Val Leu Val
 210 215 220

Leu Phe Trp Phe Leu Val Gly Gly Cys Val Val Cys Ala Leu Cys Val
 225 230 235 240

Leu Phe Val Val Phe Val Arg Ser Trp Cys Thr Ala Glu Lys Ser His
 245 250 255

His Gln Arg Thr Ser Phe Asn Arg Leu Ile Val Gly Ala Ser Pro Glu
 260 265 270

Gly Leu Arg Ala Gly Arg Ser Gly Gly Cys Ser Arg Leu Leu Phe Phe
 275 280 285

Ala Pro Trp Ala Leu Ser Lys Arg Ser Arg Tyr Leu Ala Leu Glu Gly
 290 295 300

Thr Leu Ala Pro Pro Phe Phe Phe Cys Met Ser Thr Phe Ala Phe Ile
 305 310 315 320

Glu

<210> 565

<211> 149

<212> PRT

<213> Homo sapien

<400> 565

Met His Gln Arg Pro Pro Thr Leu Pro Arg Ile Ala Phe Met Ile Glu
 1 5 10 15

Leu Lys Leu Leu Lys Val Ile His Ser Pro His Asp Arg Ala Val Pro
 20 25 30

710

Pro Ser Leu Pro Leu Cys Leu Trp Ala Pro Glu Ala Pro Leu Ile Pro
 35 40 45

Gly Arg Phe Leu Pro Pro Cys Leu His Ser Ser Leu Leu Ser Pro Leu
 50 55 60

Phe Leu Lys Leu Leu Phe Leu Thr Leu Leu Glu Ala Arg Leu Asp Asp
 65 70 75 80

Trp Leu Asn Thr Leu Tyr Leu Arg Glu Arg Leu Tyr Leu Lys Phe Glu
 85 90 95

Ile Leu Cys Thr Ser Tyr Asn Ala Gly Cys Thr Leu Ser Arg Ile Pro
 100 105 110

Ser Leu Ser Ser Ser Cys Ser Ser Leu His Thr Arg Gln Ala Gly Val
 115 120 125

Pro Cys Leu Ser Ser Leu Phe His Ala Ser His Lys Cys Tyr Val Trp
 130 135 140

Ile Leu Leu Pro His
 145

<210> 566

<211> 387

<212> PRT

<213> Homo sapien

<400> 566

Met Arg Ser Val Ser Tyr Val Gln Arg Val Ala Leu Glu Phe Ser Gly
 1 5 10 15

Ser Leu Phe Pro His Ala Ile Cys Leu Gly Asp Val Asp Asn Asp Thr
 20 25 30

Leu Asn Glu Leu Val Val Gly Asp Thr Ser Gly Lys Val Ser Val Tyr
 35 40 45

Lys Asn Asp Asp Ser Arg Pro Trp Leu Thr Cys Ser Cys Gln Gly Met
 50 55 60

Leu Thr Cys Val Gly Val Gly Asp Val Cys Asn Lys Gly Lys Asn Leu
 65 70 75 80

711

Leu Val Ala Val Ser Ala Glu Gly Trp Phe His Leu Phe Asp Leu Thr
85 90 95

Pro Ala Lys Val Leu Asp Ala Ser Gly His His Glu Thr Leu Ile Gly
100 105 110

Glu Glu Gln Arg Pro Val Phe Lys Gln His Ile Pro Ala Asn Thr Lys
115 120 125

Val Met Leu Ile Ser Asp Ile Asp Gly Asp Gly Cys Arg Glu Leu Val
130 135 140

Val Gly Tyr Thr Asp Arg Val Val Arg Ala Phe Arg Trp Glu Glu Leu
145 150 155 160

Gly Glu Gly Pro Glu His Leu Thr Gly Gln Leu Val Ser Leu Lys Lys
165 170 175

Trp Met Leu Glu Gly Gln Val Asp Ser Leu Ser Val Thr Leu Gly Pro
180 185 190

Leu Gly Leu Pro Glu Leu Met Val Ser Gln Pro Gly Cys Ala Tyr Ala
195 200 205

Ile Leu Leu Cys Thr Trp Lys Lys Asp Thr Gly Ser Pro Pro Ala Ser
210 215 220

Glu Gly Pro Thr Asp Gly Ser Arg Glu Thr Pro Ala Ala Arg Asp Val
225 230 235 240

Val Leu His Gln Thr Ser Gly Arg Ile His Asn Lys Asn Val Ser Thr
245 250 255

His Leu Ile Gly Asn Ile Lys Gln Gly His Gly Thr Glu Ser Ser Gly
260 265 270

Ser Gly Leu Phe Ala Leu Cys Thr Leu Asp Gly Thr Leu Lys Leu Met
275 280 285

Glu Glu Met Glu Glu Ala Asp Lys Leu Leu Trp Ser Val Gln Val Asp
290 295 300

His Gln Leu Phe Ala Leu Glu Lys Leu Asp Val Thr Gly Asn Gly His
305 310 315 320

Glu Glu Val Val Ala Cys Ala Trp Asp Gly Gln Thr Tyr Ile Ile Asp

712

325

330

335

His Asn Arg Thr Val Val Arg Phe Gln Val Asp Glu Asn Ile Arg Ala
 340 345 350

Phe Cys Ala Gly Asp Pro Arg Pro His Gly Pro Phe Leu Thr Thr Leu
 355 360 365

Lys Leu Asp Arg Arg Val Arg His Ala Arg Glu Val Phe Ala Pro His
 370 375 380

Phe Pro Phe
 385

<210> 567
 <211> 31
 <212> PRT
 <213> Homo sapien

<400> 567

Glu Gly Gly Ala Glu Glu Gln His Gly Arg Glu Pro Val Ser Asp Lys
 1 5 10 15

Lys Thr Lys Thr Gln Lys Leu Asn Gly Lys Val Arg Ser Leu Asn
 20 25 30

<210> 568
 <211> 178
 <212> PRT
 <213> Homo sapien

<400> 568

Met Arg Ser Val Ser Tyr Val Gln Arg Val Ala Leu Glu Phe Ser Gly
 1 5 10 15

Ser Leu Phe Pro His Ala Ile Cys Leu Gly Asp Val Asp Asn Asp Thr
 20 25 30

Leu Asn Glu Leu Val Val Gly Asp Thr Ser Gly Lys Val Ser Val Tyr
 35 40 45

Lys Asn Asp Asp Ser Arg Pro Trp Leu Thr Cys Ser Cys Gln Gly Met
 50 55 60

Leu Thr Cys Val Gly Val Gly Asp Val Cys Asn Lys Gly Lys Asn Leu
 65 70 75 80

713

Leu Val Ala Val Ser Ala Glu Gly Trp Phe His Leu Phe Asp Leu Thr
 85 90 95

Pro Ala Lys Val Leu Asp Ala Ser Gly His His Glu Thr Leu Ile Gly
 100 105 110

Glu Glu Gln Arg Pro Val Phe Lys Gln His Ile Pro Ala Asn Thr Lys
 115 120 125

Val Met Leu Ile Ser Asp Ile Val Gly Met Pro Thr Phe Ala Gly Ser
 130 135 140

Gln Glu Ser Arg Ser Gln Trp Ile Leu Glu His Ile Pro Arg Asp Trp
 145 150 155 160

Gly Glu Arg Glu Asn Pro Tyr Ser Cys Met His Leu Leu Cys Ala Glu
 165 170 175

Leu Pro

<210> 569
 <211> 90
 <212> PRT
 <213> Homo sapien

<400> 569

Met His Gln Arg Leu Ser Lys Ser Tyr Leu Arg Pro Gln Leu Leu Pro
 1 5 10 15

Arg Thr Gln Val Val Glu Ile Ile Cys Arg Leu Asn Ile Ser Thr Trp
 20 25 30

Phe Gln Gln Ala Pro Gln Ile Gln His Ile Gln Asn Arg Ser Phe Tyr
 35 40 45

Phe Leu Ser Ala Lys Pro Thr Pro Val Pro Glu His Ile Ser Gly Asn
 50 55 60

Ser Ala Ile Arg Asn Ser Tyr Phe Ile Cys Ser Leu Tyr His Leu Thr
 65 70 75 80

Leu Thr Pro Leu Ile Ile Leu Ser Thr His
 85 90

<210> 570
 <211> 43

714

<212> PRT
 <213> Homo sapien

<400> 570

Met Val Leu Phe Leu Ile Val Tyr Phe Leu Asp Asn Asp Ser Ser Glu
 1 5 10 15

Lys Phe Arg Pro Phe Val Phe Phe Phe Asn Pro Ala Pro Ser Val Lys
 20 25 30

Thr Met Ser Tyr Arg Met Ser Cys Phe Trp Ile
 35 40

<210> 571
 <211> 55
 <212> PRT
 <213> Homo sapien

<400> 571

Met Gln Leu Ser Lys Ser Ser Leu Phe Pro Ser His Leu Gln Leu Asn
 1 5 10 15

Thr Ile Ser Gln Phe Leu Phe Leu Asp Thr Ala Arg Asn Arg Pro Ser
 20 25 30

Tyr Gln Ser Ser His Phe Leu Ser Val Ser Phe Pro Asn Ser Phe Ser
 35 40 45

Gln Asn Leu Leu Gln Ile Ser
 50 55

<210> 572
 <211> 60
 <212> PRT
 <213> Homo sapien

<400> 572

Met Leu Thr Glu Leu Leu Phe Thr Ile Tyr Phe His Ile Tyr Lys Trp
 1 5 10 15

Glu Tyr Ser Ser Ser Ile Thr Phe Cys Asn Asp His Val Ile Thr Val
 20 25 30

Gly Lys Tyr Pro Tyr Asp Lys Leu Glu Ser Leu Cys Ser Ile Val Cys
 35 40 45

Ile Arg Ile Ser Leu Ile Phe Ser Ile Ser Ser Gln
 50 55 60

715

<210> 573
 <211> 51
 <212> PRT
 <213> Homo sapien

<400> 573

Met Asn Cys Thr Gln Ala Ile Ala Glu Asp Gly Ile Val Ser Tyr Pro
 1 5 10 15

Tyr Asn Leu Glu Asn Ser Pro Trp Arg Gln Asn Pro Asp Leu Leu Arg
 20 25 30

Lys Leu Gly Leu Leu Asp Ser Arg Gln Arg Ile Val Phe Pro Asn Tyr
 35 40 45

Cys Phe Leu
 50

<210> 574
 <211> 56
 <212> PRT
 <213> Homo sapien

<400> 574

Met Ala Leu Leu Glu Leu Leu Thr Ser Asn Phe Arg Phe Asp Ser Phe
 1 5 10 15

Tyr Lys Gln Phe Phe Pro Leu Val Cys Pro Met Ser Arg Arg Pro Phe
 20 25 30

Pro Val Arg Tyr Leu Cys Met Ser His Ala Ile Cys Asn Ser Ser Cys
 35 40 45

Met Asp Ala Ser Ala Ile His Thr
 50 55

<210> 575
 <211> 728
 <212> PRT
 <213> Homo sapien

<400> 575

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
 1 5 10 15

Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
 20 25 30

716

His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45

Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60

Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80

Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu
 85 90 95

Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110

Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125

His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140

Leu Thr Tyr Leu Asn Leu Ser Arg Asn Gln Leu Ser Ala Leu Pro Ala
 145 150 155 160

Cys Leu Cys Gly Leu Pro Leu Lys Val Leu Ile Ala Ser Asn Asn Lys
 165 170 175

Leu Gly Ser Leu Pro Glu Glu Ile Gly Gln Leu Lys Gln Leu Met Glu
 180 185 190

Leu Asp Val Ser Cys Asn Glu Ile Thr Ala Leu Pro Gln Gln Ile Gly
 195 200 205

Gln Leu Lys Ser Leu Arg Glu Leu Asn Val Arg Arg Asn Tyr Leu Lys
 210 215 220

Val Leu Pro Gln Glu Leu Val Asp Leu Pro Leu Val Lys Phe Asp Phe
 225 230 235 240

Ser Cys Asn Lys Val Leu Val Ile Pro Ile Cys Phe Arg Glu Met Lys
 245 250 255

Gln Leu Gln Val Leu Leu Leu Glu Asn Asn Pro Leu Gln Ser Pro Pro
 260 265 270

717

Ala Gln Ile Cys Thr Lys Gly Lys Val His Ile Phe Lys Tyr Leu Ser
 275 280 285

Ile Gln Ala Cys Gln Ile Lys Thr Ala Asp Ser Leu Tyr Leu His Thr
 290 295 300

Met Glu Arg Pro His Leu His Gln His Val Glu Asp Gly Lys Lys Asp
 305 310 315 320

Ser Asp Ser Gly Val Gly Ser Asp Asn Gly Asp Lys Arg Leu Ser Ala
 325 330 335

Thr Glu Pro Ser Asp Glu Asp Thr Val Ser Leu Asn Val Pro Met Ser
 340 345 350

Asn Ile Met Glu Glu Glu Gln Ile Ile Lys Glu Asp Ser Cys His Arg
 355 360 365

Leu Ser Pro Val Lys Gly Glu Phe His Gln Glu Phe Gln Pro Glu Pro
 370 375 380

Ser Leu Leu Gly Asp Ser Thr Asn Ser Gly Glu Glu Arg Asp Gln Phe
 385 390 395 400

Thr Asp Arg Ala Asp Gly Leu His Ser Glu Phe Met Asn Tyr Lys Ala
 405 410 415

Arg Ala Glu Asp Cys Glu Glu Leu Leu Arg Ile Glu Glu Asp Val His
 420 425 430

Trp Gln Thr Glu Gly Ile Ile Ser Ser Ser Lys Asp Gln Asp Met Asp
 435 440 445

Ile Ala Met Ile Glu Gln Leu Arg Glu Ala Val Asp Leu Leu Gln Asp
 450 455 460

Pro Asn Gly Leu Ser Thr Asp Ile Thr Glu Arg Ser Val Leu Asn Leu
 465 470 475 480

Tyr Pro Met Gly Ser Ala Glu Ala Leu Glu Leu Gln Asp Ser Ala Leu
 485 490 495

Asn Gly Gln Ile Gln Leu Glu Thr Ser Pro Val Cys Glu Val Gln Ser
 500 505 510

718

Asp Leu Thr Leu Gln Ser Asn Gly Ser Gln Tyr Ser Pro Asn Glu Ile
 515 520 525

Arg Glu Asn Ser Pro Ala Val Ser Pro Thr Thr Asn Ser Thr Ala Pro
 530 535 540

Phe Gly Leu Lys Pro Arg Ser Val Phe Leu Arg Pro Gln Arg Asn Leu
 545 550 555 560

Glu Ser Ile Asp Pro Gln Phe Thr Ile Arg Arg Lys Met Glu Gln Met
 565 570 575

Arg Glu Glu Lys Glu Leu Val Glu Gln Leu Arg Glu Ser Ile Glu Met
 580 585 590

Arg Leu Lys Val Ser Leu His Glu Asp Leu Gly Ala Ala Leu Met Asp
 595 600 605

Gly Val Val Leu Cys His Leu Val Asn His Ile Arg Pro Arg Ser Val
 610 615 620

Ala Ser Ile His Val Pro Ser Pro Ala Val Pro Lys Leu Ser Met Ala
 625 630 635 640

Lys Cys Arg Arg Asn Val Glu Asn Phe Leu Glu Ala Cys Arg Lys Leu
 645 650 655

Gly Val Pro Glu Ala Asp Leu Cys Ser Pro Cys Asp Ile Leu Gln Leu
 660 665 670

Asp Phe Arg His Ile Arg Lys Thr Val Asp Thr Leu Leu Ala Leu Gly
 675 680 685

Glu Lys Ala Pro Pro Pro Thr Ser Ala Leu Arg Ser Arg Asp Leu Ile
 690 695 700

Gly Phe Cys Leu Val His Ile Leu Phe Ile Val Leu Val Tyr Ile Thr
 705 710 715 720

Tyr His Trp Asn Ala Leu Ser Ala
 725

<210> 576

<211> 654

<212> PRT

<213> Homo sapien

719

<400> 576

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
 1 5 10 15

Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
 20 25 30

His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45

Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60

Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80

Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu
 85 90 95

Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110

Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125

His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140

Leu Thr Tyr Leu Asn Leu Arg Met Ser Ala Ala Thr Glu Ile Thr Ala
 145 150 155 160

Leu Pro Gln Gln Ile Gly Gln Leu Lys Ser Leu Arg Glu Leu Asn Val
 165 170 175

Arg Arg Asn Tyr Leu Lys Val Leu Pro Gln Glu Leu Val Asp Leu Pro
 180 185 190

Leu Val Lys Phe Asp Phe Ser Cys Asn Lys Val Leu Val Ile Pro Ile
 195 200 205

Cys Phe Arg Glu Met Lys Gln Leu Gln Val Leu Leu Leu Glu Asn Asn
 210 215 220

Pro Leu Gln Ser Pro Pro Ala Gln Ile Cys Thr Lys Gly Lys Val His
 225 230 235 240

720

Ile Phe Lys Tyr Leu Ser Ile Gln Ala Cys Gln Ile Lys Thr Ala Asp
 245 250 255

Ser Leu Tyr Leu His Thr Met Glu Arg Pro His Leu His Gln His Val
 260 265 270

Glu Asp Gly Lys Lys Asp Ser Asp Ser Gly Val Gly Ser Asp Asn Gly
 275 280 285

Asp Lys Arg Leu Ser Ala Thr Glu Pro Ser Asp Glu Asp Thr Val Ser
 290 295 300

Leu Asn Val Pro Met Ser Asn Ile Met Glu Glu Glu Gln Ile Ile Lys
 305 310 315 320

Glu Asp Ser Cys His Arg Leu Ser Pro Val Lys Gly Glu Phe His Gln
 325 330 335

Glu Phe Gln Pro Glu Pro Ser Leu Leu Gly Asp Ser Thr Asn Ser Gly
 340 345 350

Glu Glu Arg Asp Gln Phe Thr Asp Arg Ala Asp Gly Leu His Ser Glu
 355 360 365

Phe Met Asn Tyr Lys Ala Arg Ala Glu Asp Cys Glu Glu Leu Leu Arg
 370 375 380

Ile Glu Glu Asp Val His Trp Gln Thr Glu Gly Ile Ile Ser Ser Ser
 385 390 395 400

Lys Asp Gln Asp Met Asp Ile Ala Met Ile Glu Gln Leu Arg Glu Ala
 405 410 415

Val Asp Leu Leu Gln Asp Pro Asn Gly Leu Ser Thr Asp Ile Thr Glu
 420 425 430

Arg Ser Val Leu Asn Leu Tyr Pro Met Gly Ser Ala Glu Ala Leu Glu
 435 440 445

Leu Gln Asp Ser Ala Leu Asn Gly Gln Ile Gln Leu Glu Thr Ser Pro
 450 455 460

Val Cys Glu Val Gln Ser Asp Leu Thr Leu Gln Ser Asn Gly Ser Gln
 465 470 475 480

Tyr Ser Pro Asn Glu Ile Arg Glu Asn Ser Pro Ala Val Ser Pro Thr
485 490 495

Arg Pro Gln Arg Asn Leu Glu Ser Ile Asp Pro Gln Phe Thr Ile Arg
515 520 525

Arg Lys Met Glu Gln Met Arg Glu Glu Lys Glu Leu Val Glu Gln Leu
530 535 540

Arg Glu Ser Ile Glu Met Arg Leu Lys Val Ser Leu His Glu Asp Leu
545 550 555 560

Gly Ala Ala Leu Met Asp Gly Val Val Leu Cys His Leu Val Asn His
565 570 575

Ile Arg Pro Arg Ser Val Ala Ser Ile His Val Pro Ser Pro Ala Val
580 585 590

Pro Lys Leu Ser Met Ala Lys Cys Arg Arg Asn Val Glu Asn Phe Leu
595 600 605

Glu Ala Cys Arg Lys Leu Gly Val Pro Glu Glu Lys Leu Cys Leu Pro
610 615 620

His His Ile Leu Glu Glu Lys Gly Leu Val Lys Val Gly Ile Thr Ile
625 630 635 640

Gln Ala Leu Leu Asp Ile Thr Val Thr Lys Ala Leu Phe Thr
645 650

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<210> 577
<211> 696
<212> PRT
<213> Homo sapien
```

<400> 577

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
1 5 10 15

Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
20 25 30

His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
35 40 45

722

Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60

Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80

Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu
 85 90 95

Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110

Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125

His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140

Leu Thr Tyr Leu Asn Leu Ser Arg Asn Gln Leu Ser Ala Leu Pro Ala
 145 150 155 160

Cys Leu Cys Gly Leu Pro Leu Lys Val Leu Ile Ala Ser Asn Asn Lys
 165 170 175

Leu Gly Ser Leu Pro Glu Glu Ile Gly Gln Leu Lys Gln Leu Met Glu
 180 185 190

Leu Asp Val Ser Cys Asn Glu Ile Thr Ala Leu Pro Gln Gln Ile Gly
 195 200 205

Gln Leu Lys Ser Leu Arg Glu Leu Asn Val Arg Arg Asn Tyr Leu Lys
 210 215 220

Val Leu Pro Gln Glu Leu Val Asp Leu Pro Leu Val Lys Phe Asp Phe
 225 230 235 240

Ser Cys Asn Lys Val Leu Val Ile Pro Ile Cys Phe Arg Glu Met Lys
 245 250 255

Gln Leu Gln Val Leu Leu Leu Glu Asn Asn Pro Leu Gln Ser Pro Pro
 260 265 270

Ala Gln Ile Cys Thr Lys Gly Lys Val His Ile Phe Lys Tyr Leu Ser
 275 280 285

723

Ile Gln Ala Cys Gln Ile Lys Thr Ala Asp Ser Leu Tyr Leu His Thr
 290 295 300

Met Glu Arg Pro His Leu His Gln His Val Glu Asp Gly Lys Lys Asp
 305 310 315 320

Ser Asp Ser Gly Val Gly Ser Asp Asn Gly Asp Lys Arg Leu Ser Ala
 325 330 335

Thr Glu Pro Ser Asp Glu Asp Thr Val Ser Leu Asn Val Pro Met Ser
 340 345 350

Asn Ile Met Glu Glu Glu Gln Ile Ile Lys Glu Asp Ser Cys His Arg
 355 360 365

Leu Ser Pro Val Lys Gly Glu Phe His Gln Glu Phe Gln Pro Glu Pro
 370 375 380

Ser Leu Leu Gly Asp Ser Thr Asn Ser Gly Glu Glu Arg Asp Gln Phe
 385 390 395 400

Thr Asp Arg Ala Asp Gly Leu His Ser Glu Phe Met Asn Tyr Lys Ala
 405 410 415

Arg Ala Glu Asp Cys Glu Glu Leu Leu Arg Ile Glu Glu Asp Val His
 420 425 430

Trp Gln Thr Glu Gly Ile Ile Ser Ser Ser Lys Asp Gln Asp Met Asp
 435 440 445

Ile Ala Met Ile Glu Gln Leu Arg Glu Ala Val Asp Leu Leu Gln Asp
 450 455 460

Pro Asn Gly Leu Ser Thr Asp Ile Thr Glu Arg Ser Val Leu Asn Leu
 465 470 475 480

Tyr Pro Met Gly Ser Ala Glu Ala Leu Glu Leu Gln Asp Ser Ala Leu
 485 490 495

Asn Gly Gln Ile Gln Leu Glu Thr Ser Pro Val Cys Glu Val Gln Ser
 500 505 510

Asp Leu Thr Leu Gln Ser Asn Gly Ser Gln Tyr Ser Pro Asn Glu Ile
 515 520 525

724

Arg Glu Asn Ser Pro Ala Val Ser Pro Thr Thr Asn Ser Thr Ala Pro
 530 535 540

Phe Gly Leu Lys Pro Arg Ser Val Phe Leu Arg Pro Gln Arg Asn Leu
 545 550 555 560

Glu Ser Ile Asp Pro Gln Phe Thr Ile Arg Arg Lys Met Glu Gln Met
 565 570 575

Arg Glu Glu Lys Glu Leu Val Glu Gln Leu Arg Glu Ser Ile Glu Met
 580 585 590

Arg Leu Lys Val Ser Leu His Glu Asp Leu Gly Ala Ala Leu Met Asp
 595 600 605

Gly Val Val Leu Cys His Leu Val Asn His Ile Arg Pro Arg Ser Val
 610 615 620

Ala Ser Ile His Val Pro Ser Pro Ala Val Pro Lys Leu Ser Met Ala
 625 630 635 640

Lys Cys Arg Arg Asn Val Glu Asn Phe Leu Glu Ala Cys Arg Lys Leu
 645 650 655

Gly Val Pro Glu Glu Lys Leu Cys Leu Pro His His Ile Leu Glu Glu
 660 665 670

Lys Gly Leu Val Lys Val Gly Ile Thr Ile Gln Ala Leu Leu Asp Ile
 675 680 685

Thr Val Thr Lys Ala Leu Phe Thr
 690 695

<210> 578

<211> 58

<212> PRT

<213> Homo sapien

<400> 578

Met Ala Lys Cys Arg Arg Asn Val Glu Asn Phe Leu Glu Ala Cys Arg
 1 5 10 15

Lys Leu Gly Val Pro Glu Glu Lys Leu Cys Leu Pro His His Ile Leu
 20 25 30

Glu Glu Lys Gly Leu Val Lys Val Gly Ile Thr Ile Gln Ala Leu Leu
 35 40 45

725

Asp Ile Thr Val Thr Lys Ala Leu Phe Thr
 50 55

<210> 579
 <211> 65
 <212> PRT
 <213> Homo sapien

<400> 579

Leu Glu Asp Pro Val Ser Ser Pro Phe Val Cys Val Ile Pro Leu Leu
 1 5 10 15

Cys Val Ile Arg Ser Ser Ala Lys Ile Arg Ser Thr Glu Glu Lys Leu
 20 25 30

Cys Leu Pro His His Ile Leu Glu Glu Lys Gly Leu Val Lys Val Gly
 35 40 45

Ile Thr Ile Gln Ala Leu Leu Asp Ile Thr Val Thr Lys Ala Leu Phe
 50 55 60

Thr
 65

<210> 580
 <211> 536
 <212> PRT
 <213> Homo sapien

<400> 580

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
 1 5 10 15

Val Ala Thr Leu His Pro Leu His His Pro His His His His His
 20 25 30

His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45

Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60

Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80

Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu

726

85

90

95

Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110

Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125

His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140

Leu Thr Tyr Leu Asn Leu Ser Arg Asn Gln Leu Ser Ala Leu Pro Ala
 145 150 155 160

Cys Leu Cys Gly Leu Pro Leu Lys Val Leu Ile Ala Ser Asn Asn Lys
 165 170 175

Leu Gly Ser Leu Pro Glu Glu Ile Gly Gln Leu Lys Gln Leu Met Glu
 180 185 190

Leu Asp Val Ser Cys Asn Glu Ile Thr Ala Leu Pro Gln Gln Ile Gly
 195 200 205

Gln Leu Lys Ser Leu Arg Glu Leu Asn Val Arg Arg Asn Tyr Leu Lys
 210 215 220

Val Leu Pro Gln Glu Leu Val Asp Leu Pro Leu Val Lys Phe Asp Phe
 225 230 235 240

Ser Cys Asn Lys Val Leu Val Ile Pro Ile Cys Phe Arg Glu Met Lys
 245 250 255

Gln Leu Gln Val Leu Leu Leu Glu Asn Asn Pro Leu Gln Ser Pro Pro
 260 265 270

Ala Gln Ile Cys Thr Lys Gly Lys Val His Ile Phe Lys Tyr Leu Ser
 275 280 285

Ile Gln Ala Cys Gln Ile Lys Thr Ala Asp Ser Leu Tyr Leu His Thr
 290 295 300

Met Glu Arg Pro His Leu His Gln His Val Glu Asp Gly Lys Lys Asp
 305 310 315 320

Ser Asp Ser Gly Val Gly Ser Asp Asn Gly Asp Lys Arg Leu Ser Ala
 325 330 335

727

Thr Glu Pro Ser Asp Glu Asp Thr Val Ser Leu Asn Val Pro Met Ser
 340 345 350
 Asn Ile Met Glu Glu Glu Gln Ile Ile Lys Glu Asp Ser Cys His Arg
 355 360 365
 Leu Ser Pro Val Lys Gly Glu Phe His Gln Glu Phe Gln Pro Glu Pro
 370 375 380
 Ser Leu Leu Gly Asp Ser Thr Asn Ser Gly Glu Glu Arg Asp Gln Phe
 385 390 395 400
 Thr Asp Arg Ala Asp Gly Leu His Ser Glu Phe Met Asn Tyr Lys Ala
 405 410 415
 Arg Ala Glu Asp Cys Glu Glu Leu Leu Arg Ile Glu Glu Asp Val His
 420 425 430
 Trp Gln Thr Glu Gly Ile Ile Ser Ser Ser Lys Asp Gln Asp Met Asp
 435 440 445
 Ile Ala Met Ile Glu Gln Leu Arg Glu Ala Val Asp Leu Leu Gln Asp
 450 455 460
 Pro Asn Gly Leu Ser Thr Asp Ile Thr Glu Arg Ser Val Leu Asn Leu
 465 470 475 480
 Tyr Pro Met Gly Ser Ala Glu Ala Leu Glu Leu Gln Asp Ser Ala Leu
 485 490 495
 Asn Gly Gln Ile Gln Leu Glu Thr Ser Pro Val Cys Glu Val Gln Ser
 500 505 510
 Asp Leu Thr Leu Gln Ser Asn Gly Ser Gln Tyr Ser Pro Asn Glu Val
 515 520 525
 Ser Phe Leu Lys Ile Asn Gly Arg
 530 535

<210> 581

<211> 317

<212> PRT

<213> Homo sapien

<400> 581

728

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
 1 5 10 15
 Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
 20 25 30
 His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45
 Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60
 Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80
 Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu
 85 90 95
 Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110
 Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125
 His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140
 Leu Thr Tyr Leu Asn Leu Ser Arg Asn Gln Leu Ser Ala Leu Pro Ala
 145 150 155 160
 Cys Leu Cys Gly Leu Pro Leu Lys Val Leu Ile Ala Ser Asn Asn Lys
 165 170 175
 Leu Gly Ser Leu Pro Glu Glu Ile Gly Gln Leu Lys Gln Leu Met Glu
 180 185 190
 Leu Asp Val Ser Cys Asn Glu Ile Thr Ala Leu Pro Gln Gln Ile Gly
 195 200 205
 Gln Leu Lys Ser Leu Arg Glu Leu Asn Val Arg Arg Asn Tyr Leu Lys
 210 215 220
 Val Leu Pro Gln Glu Leu Val Asp Leu Pro Leu Val Lys Phe Asp Phe
 225 230 235 240
 Ser Cys Asn Lys Val Leu Val Ile Pro Ile Cys Phe Arg Glu Met Lys

729

245

250

255

Gln Leu Gln Val Leu Leu Leu Glu Asn Asn Pro Leu Gln Ser Pro Pro
 260 265 270

Ala Gln Ile Cys Thr Lys Gly Lys Val His Ile Phe Lys Tyr Leu Ser
 275 280 285

Ile Gln Ala Cys Gln Ile Lys Thr Ala Asp Ser Leu Tyr Leu His Thr
 290 295 300

Met Glu Arg Pro His Leu His Gln His Val Glu Asp Gly
 305 310 315

<210> 582
 <211> 179
 <212> PRT
 <213> Homo sapien

<400> 582

Met Asn Gly Gly Lys Tyr Ser Pro Leu Glu Ile Arg Glu Asn Ser Pro
 1 5 10 15

Ala Val Ser Pro Thr Thr Asn Ser Thr Ala Pro Phe Gly Leu Lys Pro
 20 25 30

Arg Ser Val Phe Leu Arg Pro Gln Arg Asn Leu Glu Ser Ile Asp Pro
 35 40 45

Gln Phe Thr Ile Arg Arg Lys Met Glu Gln Met Arg Glu Glu Lys Glu
 50 55 60

Leu Val Glu Gln Leu Arg Glu Ser Ile Glu Met Arg Leu Lys Val Ser
 65 70 75 80

Leu His Glu Asp Leu Gly Ala Ala Leu Met Asp Gly Val Val Leu Cys
 85 90 95

His Leu Val Asn His Ile Arg Pro Arg Ser Val Ala Ser Ile His Val
 100 105 110

Pro Ser Pro Ala Val Pro Lys Leu Ser Met Ala Lys Cys Arg Arg Asn
 115 120 125

Val Glu Asn Phe Leu Glu Ala Cys Arg Lys Leu Gly Val Pro Glu Glu
 130 135 140

730

Lys Leu Cys Leu Pro His His Ile Leu Glu Glu Lys Gly Leu Val Lys
 145 150 155 160

Val Gly Ile Thr Ile Gln Ala Leu Leu Asp Ile Thr Val Thr Lys Ala
 165 170 175

Leu Phe Thr

<210> 583
 <211> 77
 <212> PRT
 <213> Homo sapien

<400> 583

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
 1 5 10 15

Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
 20 25 30

His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45

Gly Gly Gly Ser Gly Gly Phe Asn Pro Leu Ser His Pro Leu Pro Val
 50 55 60

Thr Ser Leu Thr Pro Val Thr Leu Lys Gln Phe Ser Val
 65 70 75

<210> 584
 <211> 502
 <212> PRT
 <213> Homo sapien

<400> 584

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser
 1 5 10 15

Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
 20 25 30

His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45

Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60

731

Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80

Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu
 85 90 95

Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110

Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125

His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140

Leu Thr Tyr Leu Asn Leu Ser Arg Asn Gln Leu Ser Ala Leu Pro Ala
 145 150 155 160

Cys Leu Cys Gly Leu Pro Leu Lys Val Leu Ile Ala Ser Asn Asn Lys
 165 170 175

Leu Gly Ser Leu Pro Glu Glu Ile Gly Gln Leu Lys Gln Leu Met Glu
 180 185 190

Leu Asp Val Ser Cys Asn Glu Ile Thr Ala Leu Pro Gln Gln Ile Gly
 195 200 205

Gln Leu Lys Ser Leu Arg Glu Leu Asn Val Arg Arg Asn Tyr Leu Lys
 210 215 220

Val Leu Pro Gln Glu Leu Val Asp Leu Pro Leu Val Lys Phe Asp Phe
 225 230 235 240

Ser Cys Asn Lys Val Leu Val Ile Pro Ile Cys Phe Arg Glu Met Lys
 245 250 255

Gln Leu Gln Val Leu Leu Leu Glu Asn Asn Pro Leu Gln Ser Pro Pro
 260 265 270

Ala Gln Ile Cys Thr Lys Gly Lys Val His Ile Phe Lys Tyr Leu Ser
 275 280 285

Ile Gln Ala Cys Gln Ile Lys Thr Ala Asp Ser Leu Tyr Leu His Thr
 290 295 300

732

Met Glu Arg Pro His Leu His Gln His Val Glu Asp Gly Lys Lys Asp
 305 310 315 320

Ser Asp Ser Gly Val Gly Ser Asp Asn Gly Asp Lys Arg Leu Ser Ala
 325 330 335

Thr Glu Pro Ser Asp Glu Asp Thr Val Ser Leu Asn Val Pro Met Ser
 340 345 350

Asn Ile Met Glu Glu Glu Gln Ile Ile Lys Glu Asp Ser Cys His Arg
 355 360 365

Leu Ser Pro Val Lys Gly Glu Phe His Gln Glu Phe Gln Pro Glu Pro
 370 375 380

Ser Leu Leu Gly Asp Ser Thr Asn Ser Gly Glu Glu Arg Asp Gln Phe
 385 390 395 400

Thr Asp Arg Ala Asp Gly Leu His Ser Glu Phe Met Asn Tyr Lys Ala
 405 410 415

Arg Ala Glu Asp Cys Glu Glu Leu Leu Arg Ile Glu Glu Asp Val His
 420 425 430

Trp Gln Thr Glu Gly Ile Ile Ser Ser Ser Lys Asp Gln Asp Met Asp
 435 440 445

Ile Ala Met Ile Glu Gln Leu Arg Glu Ala Val Asp Leu Leu Gln Asp
 450 455 460

Pro Asn Gly Leu Ser Thr Asp Ile Thr Glu Arg Ser Val Leu Asn Leu
 465 470 475 480

Tyr Pro Met Gly Ser Ala Glu Ala Leu Glu Leu Gln Asp Ser Ala Leu
 485 490 495

Lys Tyr Ala Cys Leu Leu
 500

<210> 585

<211> 151

<212> PRT

<213> Homo sapien

<400> 585

Met Ala Thr Pro Gly Ser Glu Pro Gln Pro Phe Val Pro Ala Leu Ser

733

1 5 10 15
 Val Ala Thr Leu His Pro Leu His His Pro His His His His His His
 20 25 30
 His Gln His His Gly Gly Thr Gly Ala Pro Gly Gly Ala Gly Gly Gly
 35 40 45
 Gly Gly Gly Ser Gly Gly Phe Asn Leu Pro Leu Asn Arg Gly Leu Glu
 50 55 60
 Arg Ala Leu Glu Glu Ala Ala Asn Ser Gly Gly Leu Asn Leu Ser Ala
 65 70 75 80
 Arg Lys Leu Lys Glu Phe Pro Arg Thr Ala Ala Pro Gly His Asp Leu
 85 90 95
 Ser Asp Thr Val Gln Ala Asp Leu Ser Lys Asn Arg Leu Val Glu Val
 100 105 110
 Pro Met Glu Leu Cys His Phe Val Ser Leu Glu Ile Leu Asn Leu Tyr
 115 120 125
 His Asn Cys Ile Arg Val Ile Pro Glu Ala Ile Val Asn Leu Gln Met
 130 135 140
 Leu Thr Tyr Leu Asn Leu Arg
 145 150

<210> 586

<211> 51

<212> PRT

<213> Homo sapien

<400> 586

Met Leu Ala Arg Thr Arg Gly Val Val Val Glu Met Gly Glu Lys Trp
 1 5 10 15
 Met Asp Leu Asp Ile Phe Trp Ser Trp Asn Gln Gln Asn Leu Val Met
 20 25 30
 Ser Phe Met Cys Ser Leu Arg Lys Gln Glu Met Ile Lys Asp Asp Phe
 35 40 45
 Gln Val Leu
 50

734

<210> 587
 <211> 86
 <212> PRT
 <213> Homo sapien

<400> 587

Met Arg Thr Leu Gly Leu Thr Ser Met Glu Asp His Pro Ser Leu Pro
 1 5 10 15

Arg Ala Arg Asn Pro Met Ala Val Phe His Lys Pro Ala Gly Leu Leu
 20 25 30

Leu Phe Ser Leu Phe Asn Tyr Thr Ser Leu Gly Val Ala Tyr Met Leu
 35 40 45

His Leu His Phe Leu Thr Pro Ser Thr Pro Gln Ser Thr Ile Leu Leu
 50 55 60

Leu Arg Leu Leu Thr Trp Pro Leu Ser Ser Thr Leu Phe Ser Thr Leu
 65 70 75 80

Thr Cys Pro Gly Ala His
 85

<210> 588
 <211> 165
 <212> PRT
 <213> Homo sapien

<400> 588

Met Leu Leu Ala Gln Gln Ala Gly Leu Leu Arg Ser Ser Ala Ser Thr
 1 5 10 15

Leu Leu Val Asp Val Gln Phe Lys Leu His Ser Leu Cys Asp Ser Leu
 20 25 30

Lys Gly Leu Val Trp Leu Ser Leu Thr Ser Leu Ser Ser Val Pro Gly
 35 40 45

Asp Thr Leu Phe Pro Ser Ser Arg Leu Val Leu Ser Leu Ala Pro Gly
 50 55 60

Leu Leu Val Gly Lys Phe Asn Leu Leu Phe Ile Ser Ser Gly Arg Ala
 65 70 75 80

Thr Val Leu Pro Ser Gly Pro Ser Ser Gly Ile Pro Phe Ala Val Val
 85 90 95

735

Gly Ala Leu Ile Pro Leu His Val Pro Cys Ser Val Asn Pro Gly Asp
 100 105 110

Pro Arg Asp Arg Glu Leu Thr Ser Val Phe Phe Ile Trp Cys Ser Met
 115 120 125

Pro Leu Gly Val Cys Gln Thr Gly Pro Ile Met Trp Val Leu His Leu
 130 135 140

Phe Thr His Leu Pro Phe Ala Phe Arg Ile Leu Phe Pro Val Gly Asn
 145 150 155 160

Gly Phe Lys Ser Pro
 165

<210> 589
 <211> 104
 <212> PRT
 <213> Homo sapien

<400> 589

Met Phe Ser Glu Ala Leu Leu Ile His Arg Thr Tyr Leu Ala Tyr Leu
 1 5 10 15

Phe Ala Cys Leu Leu Leu Met Ser Ser Leu Thr Glu Ser Leu Leu Gln
 20 25 30

Arg Thr Thr Pro Ala Ser Arg Pro Arg Asn Val Gly Lys Gly Lys Ala
 35 40 45

Trp Leu Val Leu Val Glu Met Glu Met Leu Val Thr Val Glu Glu Cys
 50 55 60

Pro Pro Ser Asp Ser Gln Trp Gly Gly Ala Leu Gly Pro Cys His Cys
 65 70 75 80

Pro Arg Thr Ser Ala Phe Gly Cys Pro Ala Glu Arg Met Arg His Leu
 85 90 95

Ser Ser Ser Phe Trp Ser Pro Glu
 100

<210> 590
 <211> 165
 <212> PRT
 <213> Homo sapien

736

<400> 590

Met Leu Leu Ala Gln Gln Ala Gly Leu Leu Arg Ser Ser Ala Ser Thr
 1 5 10 15

Leu Leu Val Asp Val Gln Phe Lys Leu His Ser Leu Cys Asp Ser Leu
 20 25 30

Lys Gly Leu Val Trp Leu Ser Leu Thr Ser Leu Ser Ser Val Pro Gly
 35 40 45

Asp Thr Leu Phe Pro Ser Ser Arg Leu Val Leu Ser Leu Ala Pro Gly
 50 55 60

Leu Leu Val Gly Lys Phe Asn Leu Leu Phe Ile Ser Ser Gly Arg Ala
 65 70 75 80

Thr Val Leu Pro Ser Gly Pro Ser Ser Gly Ile Pro Phe Ala Val Val
 85 90 95

Gly Ala Leu Ile Pro Leu His Val Pro Cys Ser Val Asn Pro Gly Asp
 100 105 110

Pro Arg Asp Arg Glu Leu Thr Ser Val Phe Phe Ile Trp Cys Ser Met
 115 120 125

Pro Leu Gly Val Cys Gln Thr Gly Pro Ile Met Trp Val Leu His Leu
 130 135 140

Phe Thr His Leu Pro Phe Ala Phe Arg Ile Leu Phe Pro Val Gly Asn
 145 150 155 160

Gly Phe Lys Ser Pro
 165

<210> 591

<211> 189

<212> PRT

<213> Homo sapien

<400> 591

Met Phe Tyr Met Ser Arg Tyr His Ala Lys Val Leu Leu Gly Ala Ile
 1 5 10 15

Ala Ser Ala Gly Gln Pro Ala Ser Pro Leu Arg Glu Val Ser Leu Thr
 20 25 30

737

His Cys Pro Leu Leu Leu Gly Pro Ser Arg Ser His Ile Gln Gly Leu
 35 40 45

Gly His Tyr Leu Ile Asn Glu Trp Val Val Arg Met Ser Lys Gln Gly
 50 55 60

Leu Thr Gln Arg Ser Gly Val Thr Gln Pro Gln Lys Leu Arg Val Ser
 65 70 75 80

Ile Gly Ile Glu Gly Pro Arg Asn Val Phe Phe Val Asp Val Ser Leu
 85 90 95

Leu Gln Arg Thr Thr Pro Ala Ser Arg Pro Arg Asn Val Gly Lys Gly
 100 105 110

Lys Ala Trp Leu Val Leu Val Glu Met Glu Met Leu Val Thr Val Glu
 115 120 125

Glu Cys Pro Pro Ser Asp Ser Gln Trp Gly Gly Ala Leu Gly Pro Cys
 130 135 140

His Cys Pro Arg Thr Ser Gly Lys Ser Ala Arg Gly Pro Gln Pro Phe
 145 150 155 160

Pro Ala Arg Arg Pro Gly Arg Arg Leu Val Leu Thr Ser Met Arg Phe
 165 170 175

Leu Asp Gly Thr Ala Ser Leu Leu Ser Lys Pro Phe Leu
 180 185

<210> 592

<211> 86

<212> PRT

<213> Homo sapien

<400> 592

Met Arg Thr Leu Gly Leu Thr Ser Met Glu Asp His Pro Ser Leu Pro
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Arg Ala Arg Asn Pro Met Ala Val Phe His Lys Pro Ala Gly Leu Leu
 20 25 30

Leu Phe Ser Leu Phe Asn Tyr Thr Ser Leu Gly Val Ala Tyr Met Leu
 35 40 45

His Leu His Phe Leu Thr Pro Ser Thr Pro Gln Ser Thr Ile Leu Leu

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Leu Arg Leu Leu Thr Trp Pro Leu Ser Ser Thr Leu Phe Ser Thr Leu
 65 70 75 80

Thr Cys Pro Gly Ala His
 85

<210> 593
 <211> 24
 <212> PRT
 <213> Homo sapien

<400> 593

Met Tyr Leu Thr Ser Phe Leu Val Phe Ser Ser Glu Ser Arg Asp Asp
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Asp Asp Asn Val Thr Ser His Asp
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<210> 594
 <211> 30
 <212> PRT
 <213> Homo sapien

<400> 594

Met Val Ile Tyr Gln Ser Pro Leu Gln Phe Leu Thr Trp Ser Ser Thr
 1 5 10 15

Ser Arg Lys Ser Ser Phe Leu Ser Gln Arg Val Leu Gly Pro
 20 25 30

<210> 595
 <211> 94
 <212> PRT
 <213> Homo sapien

<400> 595

Met Gly Lys Asp Leu Thr Pro Ile Thr Pro Ser Ser Gly Phe Thr Ile
 1 5 10 15

Glu Leu Ala Ser Ala Phe Thr Val Val Ile Ala Ser Asn Ile Gly Leu
 20 25 30

Pro Val Ser Thr Thr His Cys Lys Val Gly Ser Val Val Ala Val Gly
 35 40 45

Trp Ile Arg Ser Arg Lys Ala Val Asp Trp Arg Leu Phe Arg Asn Ile

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Phe Val Ala Trp Phe Val Thr Val Pro Val Ala Gly Leu Phe Ser Ala
 65 70 75 80

Ala Val Met Ala Leu Leu Met Tyr Gly Ile Leu Pro Tyr Val
 85 90

<210> 596
 <211> 94
 <212> PRT
 <213> Homo sapien

<400> 596

Met Gly Lys Asp Leu Thr Pro Ile Thr Pro Ser Ser Gly Phe Thr Ile
 1 5 10 15

Glu Leu Ala Ser Ala Phe Thr Val Val Ile Ala Ser Asn Ile Gly Leu
 20 25 30

Pro Val Ser Thr Thr His Cys Lys Val Gly Ser Val Val Ala Val Gly
 35 40 45

Trp Ile Arg Ser Arg Lys Ala Val Asp Trp Arg Leu Phe Arg Asn Ile
 50 55 60

Phe Val Ala Trp Phe Val Thr Val Pro Val Ala Gly Leu Phe Ser Ala
 65 70 75 80

Ala Val Met Ala Leu Leu Met Tyr Gly Ile Leu Pro Tyr Val
 85 90

<210> 597
 <211> 82
 <212> PRT
 <213> Homo sapien

<400> 597

Ala Ser Ser Ser Pro Ala Pro Pro Gly Lys His Gly Glu Gly Arg Gln
 1 5 10 15

Glu Glu Val Gln Val Cys Pro Pro Pro Ile His Cys Pro Lys Thr Arg
 20 25 30

Trp Glu Arg Lys Glu Leu Phe Leu Glu Val Glu Leu His Val Arg Asn
 35 40 45

740

Cys Asn Gly Leu Trp Trp Ala Arg Trp Trp Pro Trp Ala Gly Ser Ala
 50 55 60

Pro Ala Arg Leu Trp Thr Gly Ala Ser Phe Gly Thr Ser Ser Trp Pro
 65 70 75 80

Gly Ser

<210> 598
 <211> 144
 <212> PRT
 <213> Homo sapien

<400> 598

Ala Gly Glu Thr Gln Arg Arg Pro Gln Cys Arg Pro Arg Ala Arg Glu
 1 5 10 15

Trp Ser Arg Ala Pro Phe Pro Tyr Arg Ala Ala Thr Pro Ala Arg Ala
 20 25 30

Ala Arg Ala Ala Ser Arg Glu Pro Pro Ala Arg Leu Pro Gly Ser Arg
 35 40 45

Gly Trp Gly Pro Gly Leu Val Gly Ala Gly Gly Ala Arg Gly Gly Gly
 50 55 60

Gly Leu Arg Pro Pro Arg Leu Leu Ala His Val Asp Leu Ala Val Ala
 65 70 75 80

Cys Arg Ala Ala Pro Leu Arg Lys Leu Asp Gly Ser Gly Arg Asp Arg
 85 90 95

Ala Leu Pro Ala Ser Ala Gly Arg Leu Leu Leu Arg Cys Ala Arg Leu
 100 105 110

Gly Trp Asp Ser Ala Gly Glu Gly Ser Cys Thr Leu Ser His Gln Ala
 115 120 125

Gln Cys Ser Arg Ala Ala Gln Arg Ile Ser Phe Leu Val Leu Arg Ala
 130 135 140

<210> 599
 <211> 151
 <212> PRT
 <213> Homo sapien

<400> 599

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Met Leu Gly Arg Gly Gln Asn Leu Pro Arg Asp Pro Glu Gly Gln Asn
 1 5 10 15

Thr Leu Glu Gly Pro Gly Ile Leu Met Ser Pro Leu Ser Pro Arg Trp
 20 25 30

Phe Ser Gly Met Glu Lys Ala Pro Cys Pro Pro Leu Glu Pro Cys Ser
 35 40 45

Arg Ala Asp Glu Thr Pro Ala Arg Pro Ala Glu His Tyr Ser Arg Met
 50 55 60

Lys Glu Ser Gln Arg Lys Arg Gln Met Cys Trp Pro Val Asn Ser Leu
 65 70 75 80

Ile Ser Asn Val Asn Gln Ile Gln Ala His Asp Ile Arg Ser Ala Ser
 85 90 95

Pro Thr Val Gly Ile Leu Cys Gly Pro Ile Val Trp Thr Val Trp Val
 100 105 110

Arg Ser Leu Trp Leu Phe Cys Asp Ala Cys Val Gly Ser Ser Leu Ser
 115 120 125

Ala Gln Lys Leu Gln Thr Leu Trp Asn Arg Phe Ser Gly Pro Val Ala
 130 135 140

Val Thr Pro Ala Leu Glu Thr
 145 150

<210> 600

<211> 127

<212> PRT

<213> Homo sapien

<400> 600

Met Ser Pro Leu Ser Pro Arg Trp Phe Ser Gly Met Glu Lys Ala Pro
 1 5 10 15

Cys Pro Pro Leu Glu Pro Cys Ser Arg Ala Asp Glu Thr Pro Ala Arg
 20 25 30

Pro Ala Glu His Tyr Ser Arg Met Lys Glu Ser Gln Arg Lys Arg Gln
 35 40 45

Met Cys Trp Pro Val Asn Ser Leu Ile Ser Asn Val Asn Gln Ile Gln

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60

Ala His Asp Ile Arg Ser Ala Ser Pro Thr Val Gly Ile Leu Cys Gly
 65 70 75 80

Pro Ile Val Trp Thr Val Trp Val Arg Ser Leu Trp Leu Phe Cys Asp
 85 90 95

Ala Cys Val Gly Ser Ser Leu Ser Ala Gln Lys Leu Gln Thr Leu Trp
 100 105 110

Asn Arg Phe Ser Gly Pro Val Ala Val Thr Pro Ala Leu Glu Thr
 115 120 125

<210> 601

<211> 30

<212> PRT

<213> Homo sapien

<400> 601

Met Cys His Ile Ala Lys Gly Lys Ser Leu Ile Ser Arg Pro Asn Phe
 1 5 10 15

Asn Gln Ile Val Asn Leu Thr His Tyr Ile Phe Val Asn Met
 20 25 30

<210> 602

<211> 191

<212> PRT

<213> Homo sapien

<400> 602

Met Arg Glu Ser Ser Ser Gly Phe Pro Ser Pro Ala Glu Val Pro Val
 1 5 10 15

Leu Ala Thr Ser Leu Pro Ile His Arg Trp Gly Arg Pro Ala Ala His
 20 25 30

Pro Pro Cys His Cys Gln Val Pro Trp Ala Ser Ser Pro His Leu Leu
 35 40 45

Ser Pro Gln Ser Ala Cys Cys Arg Trp Thr Val Lys Ile His Trp Trp
 50 55 60

Thr Val His Leu Ser Leu Val Thr Leu Arg Cys Ser Leu Arg Ile Phe
 65 70 75 80

743

Val Pro Leu Pro Gln Glu Val Val Val Ser Gln Pro Ser Cys Gln Asp
85 90 95

Leu Thr Leu Ile Val Val Tyr Gln Glu Thr Cys Arg Leu Pro Ser Tyr
100 105 110

Ser Arg His Val Gly Met Tyr Leu Thr Val Leu Leu Gln Asn Ile Asp
115 120 125

Arg His Ile Thr Asp Gly Pro Cys Leu Met Glu Ile Arg Pro Gln Leu
130 135 140

Val Gln Leu Leu Ser Gln Pro Leu Glu Pro Leu His Cys His Ser Ala
145 150 155 160

Pro His Leu Leu Leu Thr Val Ile Cys Gln Gly Arg Ser His Pro Arg
165 170 175

Ser Thr Ala Leu Ser Thr Ser Cys Leu Ser Val Ala Leu Pro Pro
180 185 190

<210> 603
<211> 134
<212> PRT
<213> Homo sapien

<400> 603

Met Glu Leu Arg Ser Arg Glu Glu Glu Leu Thr Arg Ala Ala Leu Gln
1 5 10 15

Gln Lys Ser Gln Glu Glu Leu Leu Lys Arg Arg Glu Gln Gln Leu Ala
20 25 30

Glu Arg Glu Ile Asp Val Leu Glu Arg Glu Leu Asn Ile Leu Ile Phe
35 40 45

Gln Leu Asn Gln Glu Lys Pro Lys Val Lys Lys Arg Lys Gly Lys Phe
50 55 60

Lys Arg Ser Arg Leu Lys Leu Lys Asp Gly His Arg Ile Ser Leu Pro
65 70 75 80

Ser Asp Phe Gln His Lys Ile Thr Val Gln Ala Ser Pro Asn Leu Asp
85 90 95

Lys Arg Arg Ser Leu Asn Ser Ser Ser Ser Pro Pro Ser Ser Pro
100 105 110

744

Thr Met Met Pro Arg Leu Arg Ala Ile Gln Cys Glu Leu Ser Ala Leu
 115 120 125

Pro Arg Gly Leu Leu Cys
 130

<210> 604
 <211> 43
 <212> PRT
 <213> Homo sapien

<400> 604

Met His Gln Gly Phe Phe Ser Leu Tyr Leu Glu Tyr Ser Leu Ser Ser
 1 5 10 15

Ser Ser Ser Gly Trp Leu Leu Pro Ser Phe Arg Ser Trp Val Arg Cys
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Cys Phe Ser Gly Thr Leu Cys Tyr Asn His Phe
 35 40

<210> 605
 <211> 55
 <212> PRT
 <213> Homo sapien

<400> 605

Met Lys Lys Glu Gln Met Ile Leu Arg Arg Val Pro Asp Ile Arg Lys
 1 5 10 15

Leu Thr Pro Lys Gly Thr Ser Lys Ala Asn Trp Leu Gln Arg Pro Thr
 20 25 30

Thr Arg Lys Glu Ser Ser Gly Val Gly Leu Cys Thr Gly Asp Asn Gly
 35 40 45

Arg Ile Cys Gly Cys Ser Ser
 50 55

<210> 606
 <211> 55
 <212> PRT
 <213> Homo sapien

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Met Leu Val Ser Ser Cys Ala Phe Ile Asn Leu Ala Lys Pro Glu Cys
 1 5 10 15

745

Ser Thr Phe Arg Ser Glu Val Pro Val Leu Ile Ala His Pro Tyr Ser
 20 25 30

Ile Ser Glu Ser Gly Ile Glu Thr Phe Ala Ile Tyr Tyr Phe Pro Phe
 35 40 45

His Gln His Pro Pro Thr Cys
 50 55

<210> 607
 <211> 35
 <212> PRT
 <213> Homo sapien

<400> 607

Met Leu Ile Asp Leu Leu His Cys His Ser Gln Lys Gln Trp Gln Tyr
 1 5 10 15

Phe Val Ser Ile Val Met Lys Leu Phe Ala Leu Ile Gly Phe Tyr Ser
 20 25 30

Gly Ser Ala
 35

<210> 608
 <211> 85
 <212> PRT
 <213> Homo sapien

<400> 608

Met Glu Glu Ala Ser Thr Cys Pro Ser Gly Ser Gln Ser Pro Cys Leu
 1 5 10 15

Ser Val Leu Pro Asp Gln Phe Leu Cys Met Ala Leu His Pro Ser Pro
 20 25 30

Arg Ala Phe Leu Leu Pro Ser Asp Gln Arg Ile Asp Val Glu Leu Trp
 35 40 45

Ala Glu Gln Ala Glu Leu Asn Ser Thr Glu Leu His Gln Met Arg Val
 50 55 60

Gln Asp Asn Cys Leu Phe Ser Ile Ser Pro Lys Ala Gly Ser Leu Ser
 65 70 75 80

Pro Leu Gly Ser Ser

746

85

<210> 609
 <211> 65
 <212> PRT
 <213> Homo sapien

<400> 609

Met Gly Arg Gly Ala Leu Ser Ser Cys Cys Thr Arg Gln Ala Pro Ser
 1 5 10 15

Pro Ser Cys Ser Lys Leu Glu Pro Ala Ser Cys Arg Pro Cys Gln His
 20 25 30

Pro Gly Trp Gly Arg Asp Gln Val Val Gly Glu Val Glu Lys Gly Leu
 35 40 45

Ser Gly Trp Ser Ala Ala Ala Glu Lys Gln Gln Lys Arg Asn Gly Glu
 50 55 60

Gly
 65

<210> 610
 <211> 138
 <212> PRT
 <213> Homo sapien

<400> 610

Ser Leu Glu Gly Arg Val Val Arg Arg Arg Gln Pro Pro Ser Gly Arg
 1 5 10 15

Gly Ser Phe Leu Val Thr Glu Asn Tyr Cys Pro Phe Thr Pro Gly Pro
 20 25 30

Asn Phe Pro Ser Pro Pro Pro Thr Ile His Pro Lys Thr Ala Val Ala
 35 40 45

Gly His Tyr Gln Gly Ser Gly Leu Ser Ser Arg Ser Leu Leu Arg Cys
 50 55 60

Ser Ala Ala Thr Gly Arg Gly Leu Pro Val Pro Gly Arg Pro Ala Gly
 65 70 75 80

Ala Gly Leu His Gly Glu Gly Gly Thr Gln Gln Leu Leu Tyr Glu Ala
 85 90 95

747

Gly Pro Leu Pro Leu Leu Leu Lys Ala Gly Ala Cys Phe Leu Ser Ser
100 105 110

Leu Ser Ala Pro Trp Val Gly Glu Gly Pro Gly Ser Gly Gly Ser Gly
115 120 125

Lys Gly Ile Glu Arg Leu Glu Cys Ser Ser
130 135

<210> 611

<211> 23

<212> PRT

<213> Homo sapien

<400> 611

Met Glu Lys Val Ser Pro Ile Trp Arg Gln Ser Ser Val Phe Pro Ile
1 5 10 15

Gly Asn Arg Gln Asn Lys Arg
20

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Organization
International Bureau



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14 August 2003 (14.08.2003)

PCT

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15/12, 15/63, C07K 14/435, C12Q 1/68

C12N 1/21,

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

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(71) Applicant (*for all designated States except US*): DI-ADEXUS, INC. [US/US]; 343 Oyster Point Boulevard, South San Francisco, CA 94080 (US).

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): SUN, Yongming [CN/US]; 551 Shoal Drive, Redwood City, CA 94065 (US). LIU, Chenghua [CN/US]; 1125 Ranchero Way #14, San Jose, CA 95117 (US).

(88) Date of publication of the international search report:
1 April 2004

(74) Agents: LICATA, Jane, Massey et al.; Licata & Tyrrell P.C., 66 E. Main Street, Marlton, NJ 08053 (US).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS RELATING TO HEPATIC SPECIFIC GENES AND PROTEINS

(57) Abstract: The present invention relates to newly identified nucleic acid molecules and polypeptides present in normal and neoplastic hepatic cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions containing the nucleic acid molecules, polypeptides, antibodies, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating hepatic cancer and non-cancerous disease states in hepatic, identifying hepatic tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered hepatic tissue for treatment and research.



WO 2003/066877 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/41349

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 1/21, 15/12, 15/63; C07K 14/435; C12Q 1/68

US CL : 435/6, 69.1, 320.1, 252.3; 536/23.5; 530/350

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 69.1, 320.1, 252.3; 536/23.5; 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | Database GenBank, Accession Number AL139328.8, WALL, M., Direct Submission. 04 April 2001. | 1-12 |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier application or patent published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

A document member of the same patent family

Date of the actual completion of the international search

05 September 2003 (05.09.2003)

Date of mailing of the international search report

11 DEC 2003

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

John S. Brusca

Telephone No. 703 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/41349

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-12 and SEQ ID NOS: 1 and 410

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12, drawn to polynucleotides, polypeptides, their method of making and using (1st product, 1st method of making, 1st method of using).

Group II, claim(s) 13, drawn to antibodies (2nd product).

Group III, claim(s) 14, drawn to a hepatic specific protein assay (2nd method of use).

Group IV, claim(s) 15, drawn to a hepatic cancer diagnostic assay (3rd method of use).

Group V, claim(s) 16, drawn to an assay kit (3rd product).

Group VI, claim(s) 17, drawn to a hepatic cancer therapeutic method (4th method of use).

Group VII, claim(s) 18, drawn to a vaccine (4th product).

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

In Group IV, a polynucleotide diagnostic species and a polypeptide diagnostic species
In Group V, a polynucleotide assay kit species and a polypeptide assay kit species
In Group VI, a polynucleotide therapeutic species and a polypeptide therapeutic species
In Group VII, a polynucleotide vaccine species and a polypeptide vaccine species

The claims are deemed to correspond to the species listed above in the following manner:

Claim 15 corresponds to the species of Group IV
Claim 16 corresponds to the species of Group V
Claim 17 corresponds to the species of Group VI
Claim 18 corresponds to the species of Group VII

The following claim(s) are generic: Claims 15-18 are Markush-type claims.

In addition, each Group detailed above reads on distinct Groups drawn to multiple sequences. The sequences are distinct because they are unrelated sequences, and a further lack of unity is applied to each Group. The Applicants must further elect one corresponding set of polynucleotide and polypeptide sequences for examination in the elected Group detailed above. Payment of fees for an additional invention will entitle the Applicants to examination of one additional set of sequences.

The total number of inventions was calculated based on the number of combinations that exist between the SEQ ID numbers and the total number of groups. The formula is recited below:

Total Number of Inventions = ((number of Groups + (Number of species - number of Groups)) X Total SEQ ID NOS)

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Each sequence set of polynucleotide and polypeptide lack a common special technical feature because each sequence corresponds to a different polypeptide with a different biological property. In addition PCT Rule 13.1 and Annex B do not provide for unity of invention between two or more different products, methods of making, or methods of using that share a special technical feature.

INTERNATIONAL SEARCH REPORT

PCT/US02/41349

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The species use or comprise compositions with different structures that produce different biological effects.

Continuation of B. FIELDS SEARCHED Item 3:

GenEMBL, GenSeq, Issued and Published US Patent sequence databases, EST databases
search terms: SEQ ID NOS: 1 and 410

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